Synthesis of γ-Diimine and Iminoisoindoline ligands for Applications in Palladium and Aluminum Coordination Chemistry and Catalysis

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Saskatoon

By

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MAY THE LORD GOD ALMIGHTY BLESS YOU ALL!

Dedication

This thesis is dedicated to my late mom, **Elita Nkholoma Chitanda**; we were just getting to know each other better when you were taken away to be with the Lord in 2005.

May Your Soul Rest in Eternal Peace

All things were made by Him;

and without Him was not anything made

that was made.

- John 1:3

Abstract

This work began with the synthesis and full characterization of a novel γ-diimine ligand, (2,6-$^{i}Pr_2C_6H_3N{=}CH)_2C_6H_4$, from the reaction of *o*-phthaladehyde and the bulky aniline, 2,6-diisopropylaniline. It was observed that any *di-ortho*-substituted aniline with less bulky groups than isopropyl groups resulted in formation of the corresponding iminoisoindolines. Reaction of the γ-diimine ligand with $PdCl_2$ did not result in a seven-membered coordination complex, but in non-palladacyclic complex [(γ-diimine)PdCl(μ-Cl)]$_2$. Whereas reaction with $Pd(OAc)_2$ gave an S-shaped five-membered trinuclear palladacyclic complex, {1,2-(2,6-$^{i}Pr_2$-$C_6H_3N{=}CH)_2$-C_6H_3]Pd(μ-$OAc)_2\}_2$Pd. These complexes were found to be active precatalysts for Heck and Suzuki coupling reactions giving TONs of up to 10^4 and 86 for aryl bromides and aryl chlorides, respectively.

On the other hand, a series of neutral and cationic seven-membered aluminum coordination complexes were obtained from the reaction of γ-diimine with a variety of aluminum species ($AlMe_3$, $AlMe_2Cl$, $AlMeCl_2$ and $AlCl_3$). The synthesis and characterization of these complexes are exemplified.

Also illustrated in this thesis is the synthesis and characterization of a series of air- and moisture-stable iminoisoindoline-based palladacyclic compounds of the general formula, [(iminoisoindoline)Pd{μ-OAc}]$_2$. These six-membered palladacyclic complexes were obtained through a simple two-step protocol as analytically pure solids. Phosphine-ligated mononuclear palladacycles of the general formula, [Pd(iminoisoindoline)X(PR_3)], (X= OAc or Cl, R = Ph or Cy), are also described. Dinuclear palladacycles were also found to be active for the Heck and Suzuki C-C coupling reactions. TONs of up to 10^6, 10^5 and 60 were observed for coupling of iodobenzene, *p*-acetylbromobenzene and *p*-chlorobenzaldehyde, respectively with butylacrylate in the Heck coupling reaction.

In addition, the syntheses and characterization of mixed iminoisoindolines, where the two aryl groups of the ligand contain different substituents, and their corresponding six-membered imine-based [CN] palladacycles of the general formula [(N,N'-diaryliminoisoindoline)Pd{μ-OAc}]$_2$ are described.

All complexes were characterized by standard spectral methods such as mass spectrometry, X-ray crystallography, elemental analysis, ^{1}H NMR, ^{13}C NMR and IR spectroscopies.

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List of Abbreviations

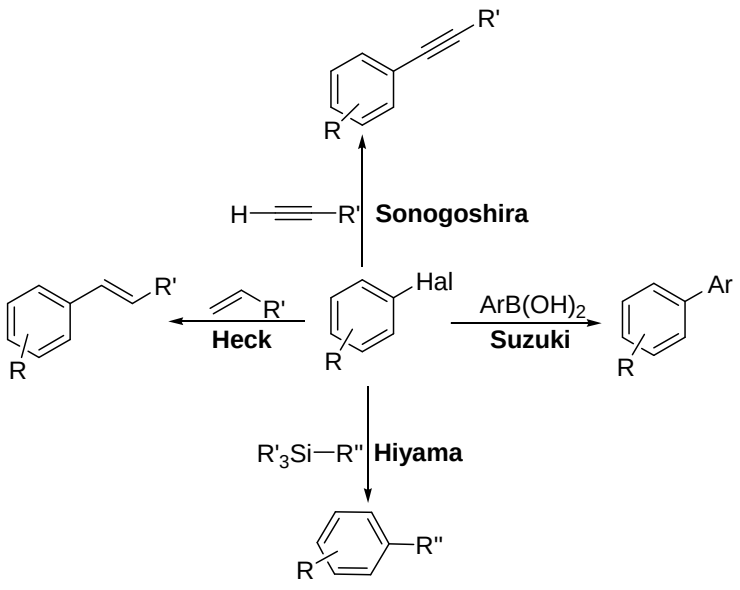
acacH	Acetylacetone
acac	Acetylacetonate
Ac	Acetyl
Ar	Aryl
BIAN	bis(aryl)acenaphthenequinonediimine
Bn	Benzyl
Bu	Butyl
*t*Bu	*tert*-Butyl
C-C	Carbon-carbon
Cy	Cyclohexyl
^{13}C NMR	Carbon 13 Nuclear Magnetic Resonance
d	Doublet
DAB	1,4-diazabutadienes
Dba	dibenzylideneacetone
DMA	Dimethylacetamide
EI	Electronic Impact Ionization
Equiv	Equivalent
Et	Ethyl
Et_2O	Ether
h	Hour
^{1}H NMR	Proton Nuclear Magnetic Resonance
HRMS	High Resolution Mass Spectrometry
HMPT	Hexamethylphosphotriamide
Hz	Hertz
*i*Pr	Isopropyl
IR	Infrared spectroscopy
J	Coupling constant
m	Multiplet
Me	Methyl
min	Minute
NMR	Nuclear Magnetic Resonance
Np	Naphthyl
OAc	Acetate
OTf	triflate
PCy_3	Tricyclohexylphosphine
Ph	Phenyl
^{31}P NMR	Phosphorus 31 Nuclear Magnetic Resonance
PPh_3	Triphenylphosphine
s	Singlet
sept	Septet
TBAB	Tetrabutylammoniumbromide
TFA	Triflouroacetate
TOF	Turnover frequency (h^{-1})
Tol.	Toluene

TON.....Turnover number
t .....Triplet
δ.....Chemical Shift

1. Introduction

1.1 Applications of Palladium-based Compounds

Palladium and palladium-based compounds have found many applications, including automotive and environmental catalysis, cancer treatment, and as catalysts/reagents in organic synthesis.[1-4] Palladium species that are used as homogeneous catalyst precursors typically have ligands coordinated to them. With regard to palladium, ligands are usually neutral or monoanionic Lewis bases that modify the electronic and steric environment around the metal centre, thereby dictating the reactivity of the complex formed. Consequently, designing ligands with favorable electronic and steric properties plays a vital role in catalysis.[2]



Scheme 1.1. Examples of carbon-carbon coupling reactions catalyzed by palladium-based compounds

Palladium-based compounds are mainly used in organic transformations, especially in carbon-carbon (C-C) cross-coupling reactions such as the Heck, Suzuki, Hiyama and Sonogashira

reactions (Scheme 1.1).[5] The resultant compounds from the C-C coupling reactions find applications in the pharmaceutical industry and usually contain palladium residue. Consequently, there is need to design and synthesize highly active complexes that give very high turnover numbers (TON, moles of product per mol of catalyst) under very low catalyst loading, thereby reducing the amount of metallic palladium in the final product.[6]

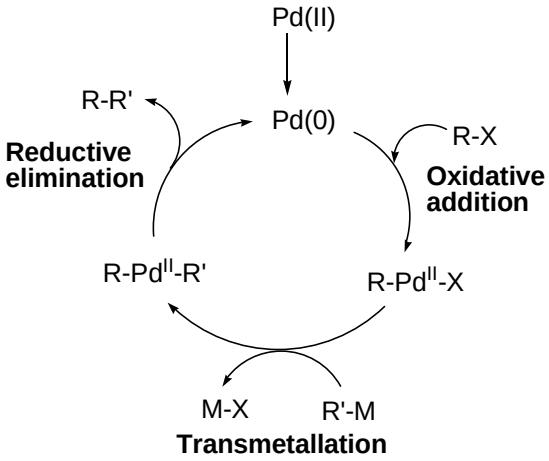


Figure 1.1. Pd(II)-Pd(0) pathway for C-C coupling reactions

Most well-established palladium catalyzed C-C cross-coupling reactions are explained on the basis of a Pd(0)/Pd(II) redox cycle. The reaction begins with active palladium in its zero-valent state, which is either directly employed, or more commonly generated in-situ from reduction of a Pd(II) precatalyst. The Pd(0) species then readily undergoes oxidative addition with one of the coupling partners (R-X, usually R = phenyl, X = halide) to form a (R)(X)Pd(II) complex. Transmetallation takes place when the other coupling partner (M-R', M = metal R' = aryl, alkyl, alkene, alkyne) is added to give an M-X and (R,R')Pd(II) complex. Complex (R,R')Pd(II) then undergoes reductive elimination to generate the final desired organic product (R-R') and a Pd(0) species, which is ready to start another cycle (Figure 1.1). A Pd(II)/Pd(IV)

redox cycle has also been suggested for some C-C coupling reactions, however this pathway is not well established.[7-10]

The rates of the oxidative addition of organohalides to Pd(0) decrease in the order C-I > C-Br >> C-Cl >> C-F. Organofluorides are usually regarded as inert towards oxidative addition, especially for palladium. Similarly, organochlorides were regarded as being unreactive towards oxidative addition; however, in the last decade there has been much progress in developing Pd systems capable of coupling organochlorides. TONs for organochlorides remain substantially lower than their bromo- or iodo-counterparts typically ranging from 10 to 10^2, although higher TONs have also been reported. This is in contrast to the coupling of aryl iodides and aryl bromides where TONs of 10^6 and 10^5, respectively have been achieved. In most cases, additions of tetra-*n*-butylammonium bromide, TBAB (referred to as Jeffery conditions),[11-13] are required to achieve such high TONs. Coupling of organochlorides is especially desirable given that organochlorides are much more abundant than their bromo- or iodo-analogues and significantly cheaper to purchase. Therefore, catalysts capable of achieving higher TONs for the coupling of organochlorides, especially at reduced temperature, are desirable. Finding catalysts to achieve these goals still remains to be a challenge.[7, 14, 15]

The following sections of this chapter are primarily concerned with the coordination chemistry and catalytic applications in C-C cross-coupling reactions of palladacycles and other diimino-based palladium complexes. Additionally, the introduction will include the chemistry of diimine ligands with alkylaluminum species to form either neutral or cationic aluminum compounds.

1.2 Palladacycle Formation and Applications

A palladacycle can be defined as any palladium compound containing at least one anionic Pd-C bond intramolecularly stabilized by one or more neutral donor atoms. These cyclic organometallic compounds generally consist of five- or six-membered rings; however, three- to nine-membered rings are also known. Within the ring, palladium is coordinated to a carbon atom and stabilized by intramolecular coordination via one or two neutral donor atoms, most commonly phosphorus, oxygen, sulfur, or nitrogen. It is important to note that coordination complexes of palladium in which a palladium atom is incorporated into a cyclic structure but does not contain at least one Pd-C bond are usually not referred to as palladacyclic species (Figure 1.2).[2]

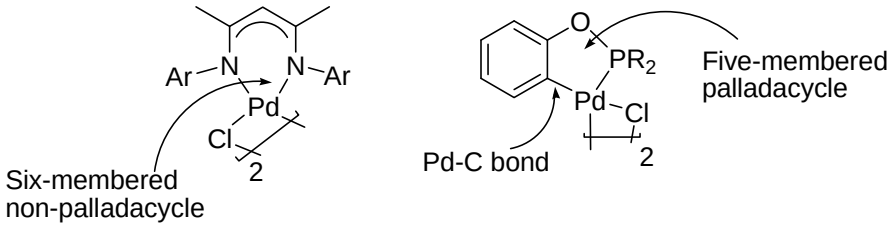
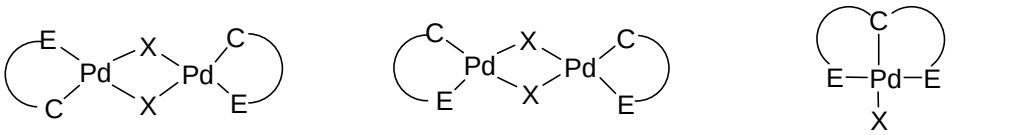


Figure 1.2. Examples of a non-palladacyclic and a palladacyclic complex

Ligands exploited in palladacycles can be classified in two categories; bidentate and tridentate ligands. Bidentate ligands ([CE], E = P, O, S, N) are mono-anionic four-electron donors, which usually form halide or acetate bridged dinuclear species. These dinuclear species can exist in two geometrical isomers (*cisoidal* {*syn*} and *transoidal* {*anti*} conformations) as shown in Figure 1.3. Tridentate ligands ([ECE], E = P, O, S, N) are mono-anionic six-electron donors, which form pincer-type palladacycles. In both cases the metallated carbon is usually an

sp^2-hybridized aromatic carbon [Pd-C_{sp2}], however sp^2 [σM-C_{sp2}] vinylic carbons and sp^3 [σM-C_{sp3}] benzylic or aliphatic carbons also exist.[2]



Transoid-palladacycle (*anti*) *Cisoid*-palladacycle (*syn*) Pincer-type palladacycle

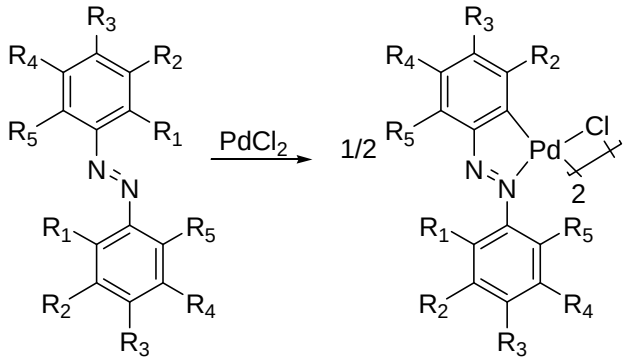
E = P, O, S, N, Se

X = Cl, Br, I, OAc.

Figure 1.3. General structures of dinuclear and mononuclear palladacycles[2]

There are three basic synthetic strategies for palladacycle formation; directed C-H bond activation, transmetallation and oxidative addition of the ligand precursor. The direct activation of a C-H bond in a ligand system is the most desirable route as the neutral ligand can be directly added to Pd. This method often requires minimal workup and avoids the need to synthesize an organometallic triflate or halide derivative. The most common requirement for the ligand to undergo direct C-H activation is an *ortho*-positioned C-H bond on an arene, where formation of the anionic Pd-C bond forms. Hence, the process is also referred to as *ortho*-palladation.[2, 16]

The first palladacycles were synthesized through a directed C-H bond activation method and were reported in 1965 by Cope *et al.* after reacting azobenzene derivatives with $PdCl_2$ as shown in Scheme 1.2.[17] All three palladacyclic complexes **1a-1c** were obtained in good to excellent yields and had satisfactory micro-analytical data; however, no solid state structures were reported.



1a: R_1 -R_5 = H

1b: R_1 = R_5 = R_3 = H, R_2 = R_4 = CH_3

1c: R_1 -R_4 = H, R_5 = C_2H_5

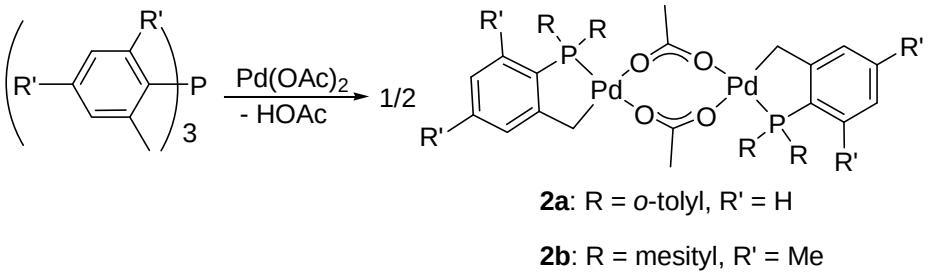
Scheme 1.2. The first examples of palladacycles by Cope *et al*.[17]

Palladacycles are powerful catalysts for the synthesis of new C-C bonds and are among the most active systems for important C-C bond forming reactions such as the Suzuki and Heck coupling reactions. They therefore represent an increasingly important class of organometallic compounds.[16, 18-21]

1.2.1 [CP] and [PCP] Palladacycles

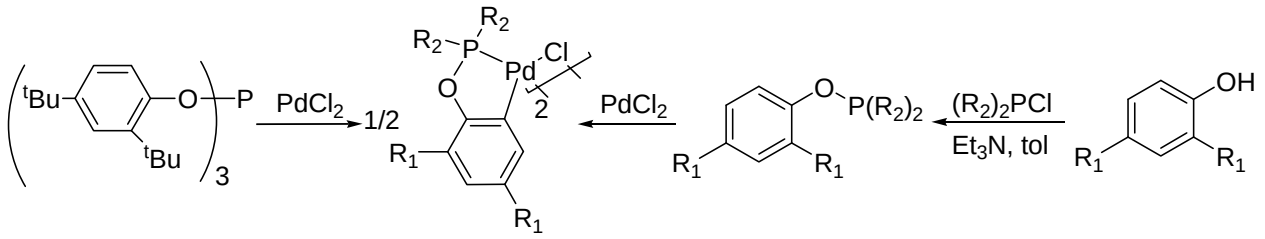
Until 1995, palladacycles were considered only to be intermediates in catalytic reactions.[22, 23] It was Herrmann *et al.* who isolated a previously known [CP] palladacycle and were the first to test it in the Heck coupling reaction. Complexes **2a**-**2b** were synthesized by the reaction of $Pd(OAc)_2$ with commercially available tris(*o*-tolyl)phosphine in toluene in 93% yield, as shown in Scheme 1.3.[24, 25] Solid-state structures showed dinuclear molecules in a closed book conformation with the ligands stacked on top of each other. Investigation in the Heck coupling reaction of aryl bromides with olefins revealed very high activities of 2.0×10^4 turnover numbers

(TON). These results were the best results reported in the Heck coupling reaction as of 1995, subsequently generating interest in applications of palladacycles for C-C coupling reactions.



Scheme 1.3. Synthesis of a [CP] palladacycle for C-C coupling reaction by Herrmann *et al*.[24, 25]

In 1998, Bedford *et al.* synthesized a series of phosphinite-based palladacyclic complexes in either one or two step protocols. Thus, treatment of phosphinite ligands with $PdCl_2$ precursors gave dinuclear chloride-bridged palladacycles **3a**-**3d** in good to excellent yields (50-96%) as shown in Scheme 1.4.[26, 27] Activity of these complexes towards the Suzuki and Heck coupling reaction was tested. In the Suzuki coupling reaction of 4-bromoacetophenone and phenylboronic acid, complex **3a** gave a TON of 10^6 and a turnover frequency (TOF) of 9×10^5 h^{-1}. The catalytic activity, using the same substrates but employing a mixture of complex **3b** with one more equiv of the corresponding ligand, increased almost five fold (TON = 4.8×10^6) compared to **3a**.



3a: $R_1 = {}^{t}Bu$, $R_2 = OC_6H_3\text{-}2,4\text{-}{}^{t}Bu_2$ (96%)

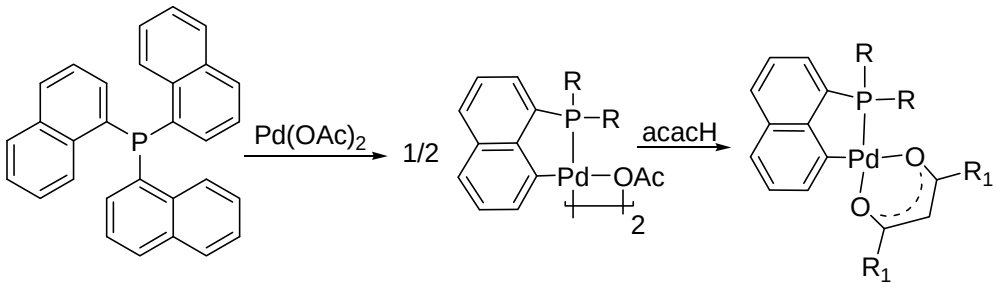
3b: $R_1 = {}^{t}Bu$, $R_2 = Ph$ (52%)

3c: $R_1 = {}^{t}Bu$, $R_2 = {}^{i}Pr$ (50%)

3d: $R_1 = H$, $R_2 = Ph$ (65%)

Scheme 1.4. Synthesis of C-P palladacycles by Bedford *et al*.[26, 27]

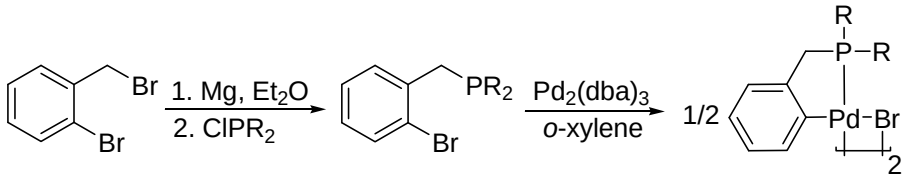
While in the Heck reaction, coupling of 4-bromoacetophonone with styrene gave a TON of 5.8 x 10^6 and TOF of 2.9 x 10^5 h^{-1}. This is so far the highest recorded TON after that of 1.2 x 10^6 reported by Shaw for coupling of iodobenzene with methylacrylate using mononuclear palladacyclic complex **4** (Scheme 1.5). Palladacycle **4** was obtained from the reaction of PNp_3, (Np = naphthyl) with $Pd(OAc)_2$, followed by reaction the resultant dimer with 2 equiv of acetylacetone (acacH) (Scheme 1.5).[28]



4: R = naphthyl, $R_1 = CF_3$

Scheme 1.5. Synthesis of [CP] palladacycles synthesized by Shaw[28]

Gibson *et al.* were interested in whether the nature of the Pd-C bond was important in determining catalyst efficiencies, so they synthesized complexes similar to Herrmann's catalyst **3b**, but with a metallated benzyl ligand.[29] Thus, reaction of tertiary *o*-bromobenzylphosphine ligands with $Pd_2(dba)_3$, dba = dibenzylideneacetone, underwent metallation to form bromide-bridged dinuclear complexes as shown in Scheme 1.6. These complexes exhibited efficient cross-coupling catalytic activity in the Heck as well as the Suzuki coupling reactions. For instance, coupling of *p*-bromoacetophenone with butyl acrylate using complexes **5a**-**5b** gave TONs of up to 3.7 x 10^6. Results from the Suzuki coupling of bromides and chlorides showed reduced activities compared to Herrmann's complex **3b**. It was concluded that replacement of the oxygen in the palladacyclic ring with methylene group is unfavorable to the overall performance of the catalyst.



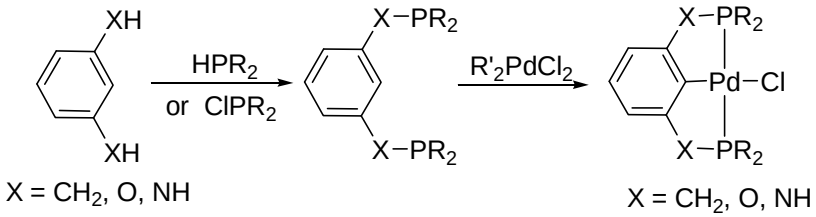
5a: R = Ph

5b: R = ^{t}Bu

Scheme 1.6. Synthesis of [CP] palladacycles for C-C coupling reaction[29]

[PCP] pincer complexes were first introduced by Moulton and Shaw in 1976 and have a structure of type **6** (Figure 1.4) in which phosphine donor arms are connected to central aromatic ring through a methylene group to form a double five-membered palladacycle.[30] The complex was obtained in 75% yield using a general synthesis as shown in Scheme 1.7. Additional examples of complexes with such connectivity also exist in literature (**7-8**).[31-33] Other [PCP] complexes with a linker other than carbon atoms have been reported; generally, oxygen and

nitrogen linkers are synthesized from an alcohol and an amine group, respectively, as shown in Scheme 1.7.



Scheme 1.7. General synthesis of C, O and N linked palladacycles[30]

As shown in Figure 1.4, complexes **9** and **10**, and **11** have symmetrically positioned oxygen and nitrogen linkers, respectively.[34-37] Other complexes have mixed linkers. For instance, **12** has one oxygen and one carbon linker, while complex **13** has one oxygen and one nitrogen linker.[37, 38] Complexes of type **14** also exist in which the ring sizes (five- and six-membered) are different due to the difference in the two linkers and represent complexes where one donor is a phosphinite and the other is a phosphine.[38] In 2006, another interesting PCP pincer complex **15** was reported in which the two palladacycles are built on fully aliphatic backbone.[39] Venanzi *et al.* reported the only example of a PCP pincer ligand forming a double six-membered palladacycle **16**.[40]

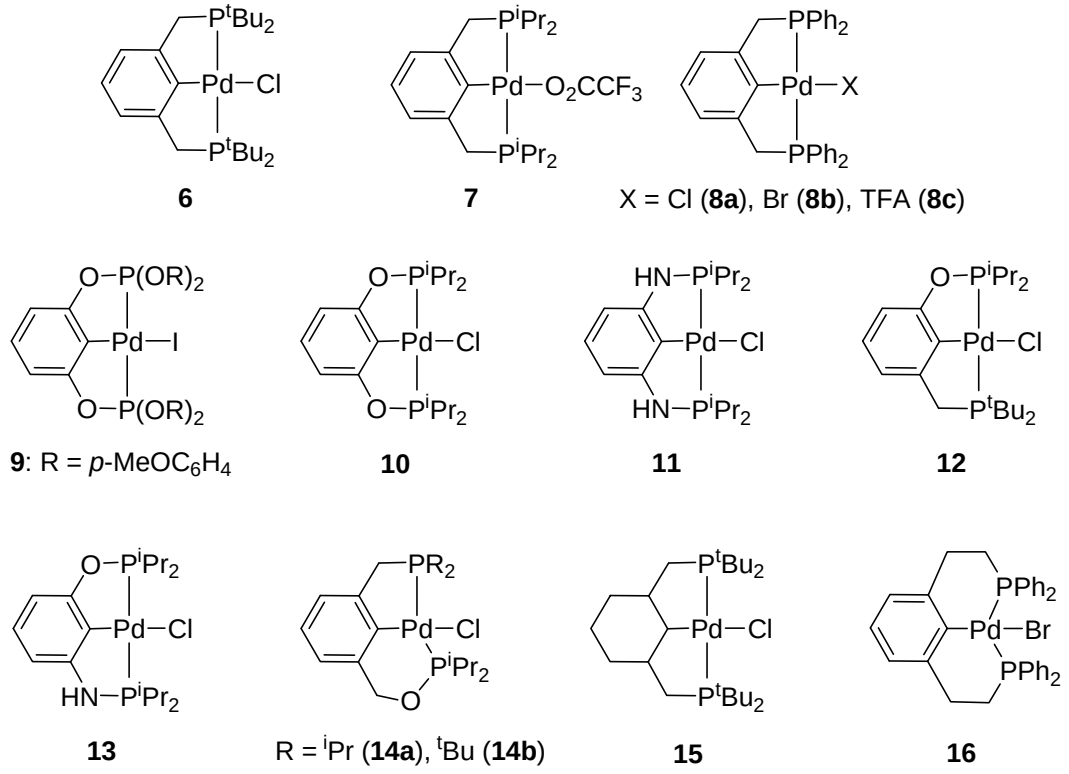


Figure 1.4. Examples of different types of pincer complexes

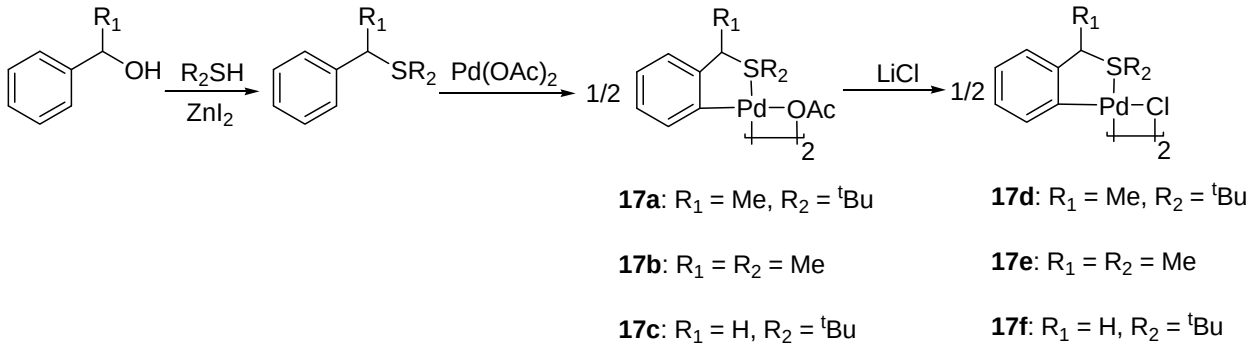
[PCP] pincer complexes were not applied as catalyst precursors until 1997 when Milstein and co-workers used pincer complex **7** in the Heck coupling reaction of bromobenzaldehyde with methylacrylate to give TONs of 1.1 x 10^5.[29] Using bis(phosphinato) pincer complex **9**, Shibasaki *et al.* reported extraordinarily high TONs of up to 8.9 x 10^6 when iodobenzene was reacted with *n*-butylacrylate in the presence of hydroquinone.[34] However, when aryl bromides and aryl chlorides were reacted with styrene, in the presence of **9**, no activity was observed.

1.2.2 [CS] and [SCS] Palladacycles

Syntheses of [CS] palladacycles have been known since the early 1970's, but their application in C-C coupling reactions was not reported until the early 2000's. Gruber *et al.*

reported the synthesis and catalytic activities of a series of sulfur-based [CS] palladacycles **17a-17d** and **18** (Scheme 1.8).[41] They also conducted catalytic studies on pincer [SCS] complex **18** that was previously reported by Shaw *et al.* (Figure 1.5).[42]

The general synthesis of **17a-17f** is shown in Scheme 1.8. Starting with the reaction of benzyl alcohol and alkylmercaptan under refluxing conditions and in the presence of ZnI_2, thioethers were obtained in good yields, which were subsequently reacted with $Pd(OAc)_2$ to give acetate-bridged dinuclear palladacycle **17a**. Reaction of LiCl with acetate-bridged complexes gave their respective chloride-bridged dimeric complexes (**17d-17f**). The Suzuki coupling reaction of 4-bromotoluene and phenylboronic acid was found to be promoted by all the palladacycles.[43,44] However, higher TON of up to 4.7×10^3 were only obtained by those palladacycles with bulky R-groups on the S atom (**17a**, **17d**, **17f** and **18**) in the presence of 20% tetra-*n*-butylammonium bromide. Using palladacycle **17d**, sterically demanding substrates such as 2-bromomesitylene and 2-tolylboronic acid were coupled to give a TON of 130 for the desired product, (2,2',4,6-tetramethylbiphenyl). The highest TON obtained for coupling phenylboronic acid with an activated aryl chloride (*p*-nitrochlorobenzene) using **17d** was 190. In the Heck reaction, the highest TON of 1.8×10^6 was reported for coupling of iodobenzene and methylacrylate using **17d.** Performing the same reaction with bromobenzene and *p*-nitrochlorobenzene gave lower activity with TONs of 60 and 410, respectively.[41]



Scheme 1.8. General synthesis of [SC] palladacycles[43,44]

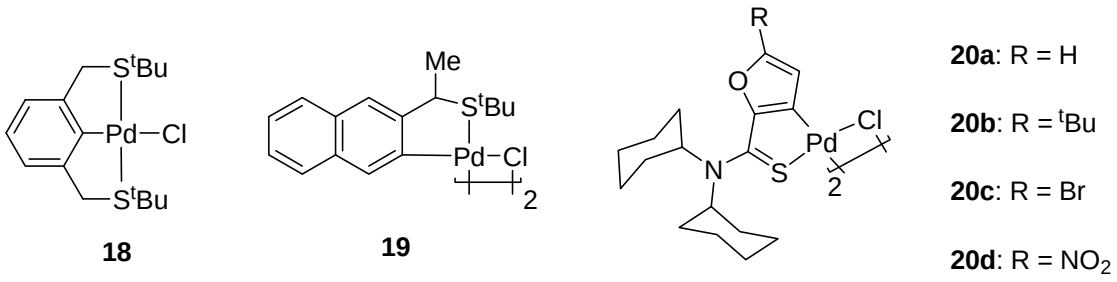
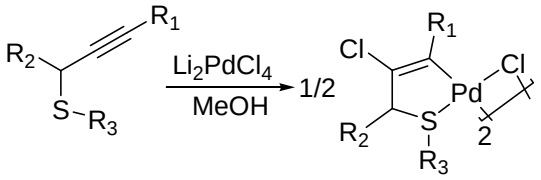


Figure 1.5. Other examples of [SC] and [SCS] palladacycles for C-C coupling reactions

In another article, Xiong *et al.* reported on the synthesis of a series of furacarbothioamide-based palladacycles (**20a**-**20d**) (Figure 1.5). They also used these complexes in the Suzuki coupling reaction as well as the Heck coupling reaction under aerobic conditions.[45] Accordingly, they reported that among the complexes prepared, complex **20a** was the best catalyst precursor. The highest TON in the coupling of a series of iodobenzene and olefin substrates (Heck reaction) at 120 ^{o}C for 1-3 h was 9.0 x 10^3. Activation of bromides required higher catalyst loading, longer reaction time and some required the addition of tetra-*n*-butylammonium bromide to push the reaction to completion. However, activation of aryl chloride substrates was not observed. Since these complexes were air- and moisture-stable, Suzuki coupling reactions were conducted under aerobic conditions with the highest TON being 910.

Dupont *et al*. reported a synthesis of [SC] palladacycles employing a series of propargyl thioethers as starting materials. Thus, treatment of Li_2PdCl_4 with propargyl thioether resulted in air-stable five-membered chloride-bridged palladacyclic complexes **21-24** as shown in Scheme 1.9 and Figure 1.6.[46, 47] It was observed that the size of the terminal alkyne substituents had an effect on the formation of the desired palladacycles. For instance, alkynes with bulky terminal (R_1) groups (^{t}Bu or $SiMe_3$) did not result in cyclopalladated complexes, instead only adducts of the form $PdCl_2(alkyne)_2$ were observed. While those with hydrogen as the terminal group (R_1 = H) gave low yields of the desired palladacycle in addition to unidentified mixtures of organic/organometallic compounds.



Scheme 1.9. General synthesis of [SC] palladacycles[46, 47]

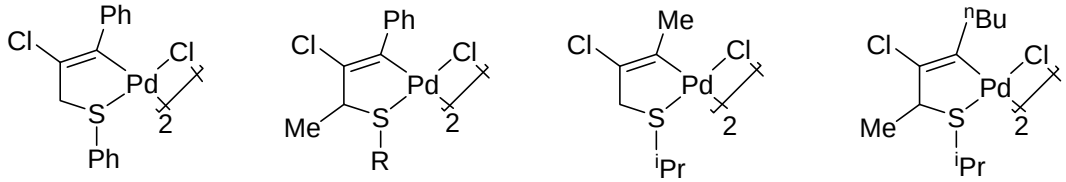
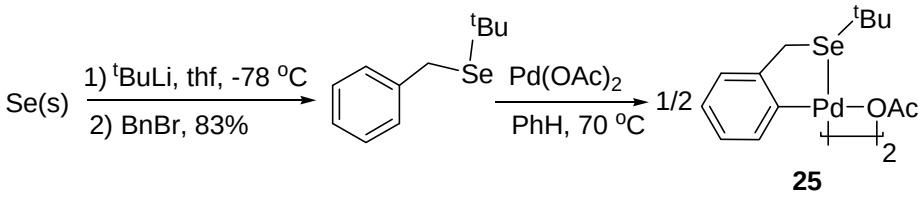


Figure 1.6. Examples of [SC] palladacycles by Dupont *et al.*[46, 47]

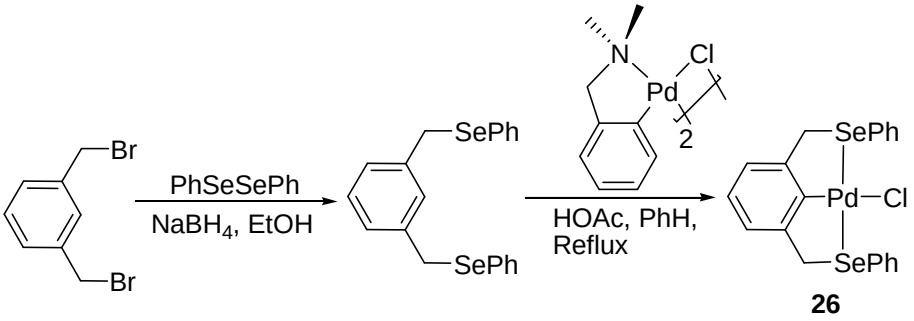
1.2.3 Five- and Six-membered [SeC], [SeCSe] and [OC] Palladacycles

Selenium- ([SeC] and [SeCSe]) and oxygen- [OC] based palladacycles, although known, have relatively few examples. Yao Q. *et al.* reported the synthesis and catalytic activity for the Heck coupling reactions of palladacycles **25** and **26**.[48] The syntheses of complexes **25** and **26** are shown in Schemes 1.10 and 1.11, respectively. Lithiation of selenium powder and subsequent reaction with benzyl bromide gave the desired ligand (83% yield), which was then treated with $Pd(OAc)_2$ to yield an acetate-bridged selenium-based palladacycle **25** in 91% yield (Scheme 1.10). On the other hand, reaction of α,α′-dibromo-*m*-xylene with diphenyl diselenide in presence of $NaBH_4$ gave the desired ligand in excellent yields (96%), which upon reaction with a $PdCl_2$ source, (a [CN] palladacycle), gave selenium-based pincer palladacycle **26** in 45% yield (Scheme 1.11). Both selenium-based palladacycles showed high catalytic activities, with **26** exhibiting higher activity giving TON of up to 2.4 $x10^5$ for phenyl bromide and *n*-butyl-acrylate, while **25** gave a TON of 1.2 $x10^5$ for the same reactions and under identical reaction conditions. Activation of *p*-bromobenzaldehyde with complex **25** in the presence of *n*-butylacrylate gave a TON of 1.7 x 10^6 which outperforms its sulfur analog **17b** (TON of up to 3.3 x 10^4 for *p*-bromobenzaldehyde in the presence of *n*-BuNBr).[41] Similarly, they reported that complex **25** is even more reactive than its phosphine analogues, for similar Heck reactions, such as Herrmann's (**2a**) and Gibson's (**3a**) *P*-palladacycles. [24,25,26,27]



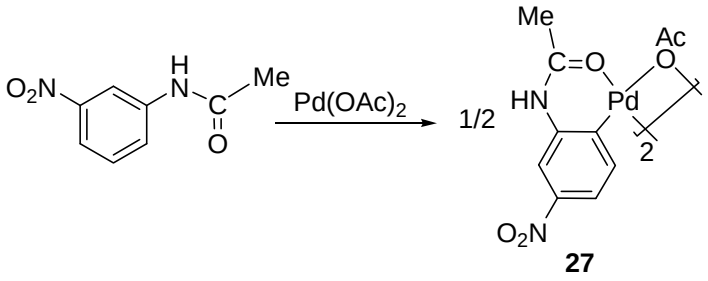
25

Scheme 1.10. Synthesis of a [SeC] palladacycles[48]



Scheme 1.11. Synthesis of a [SeCSe] pincer palladacycle[48]

Oxygen-based acetate-bridged [OC] palladacyclic complex **27** was first synthesized and reported by Horino *et al.* in 1981 from the reaction of acetanilide and $Pd(OAc)_2$ under reflux in 99.3% yield (Scheme 1.12).[49] In 2001, Beletskaya *et al.* tested complex **27** for the Heck coupling reaction of styrene and ethyl acrylate with iodobenzene to give TON of 1 x 10^3 and 930, respectively.[50] No catalytic studies with aryl bromides and aryl chlorides were reported.



Scheme 1.12. Synthesis of an [OC] palladacycle[49]

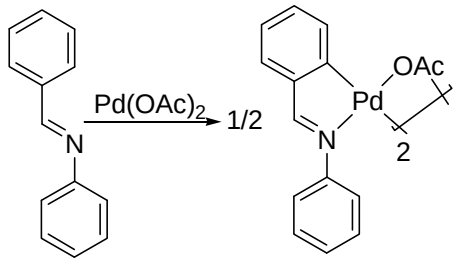
1.3 [CN] and [NCN] Palladacycles

[CN] and [NCN] palladacycles are the most extensively studied cyclometallated compounds in the literature. Palladacycles of four-, five-, and six-membered or larger rings have been reported.[2] The nitrogen donor atom usually is part of different compounds such as imines,

amines, pyridines, oxazolines and amidines. As mentioned earlier (Section 1.2), the first N-based palladacycle was synthesized in the 1960s using azobenzene as the ligand.[17] In this review however, focus will be on five and six-membered imine (=NR), amine ($-NR_2$) and pyridine-based palladacycles.

1.3.1 Imine-based [CN] and [NCN] Palladacycle and Catalysis

The first reports on imine-based palladacycles were recorded in the late 1960s. In 1969, Molnar *et al*. obtained a five-membered imine [CN] palladacycle **28** through the reaction of benzylaniline with $Pd(OAc)_2$ (Scheme 1.13).[51]

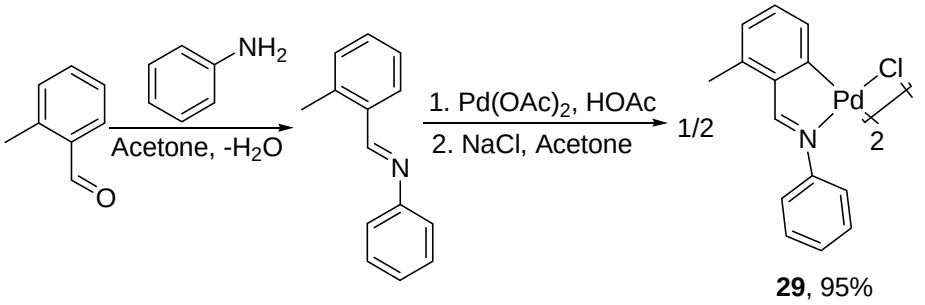


28

Scheme 1.13. Synthesis of five-membered acetate-bridged palladacycle by Molnar *et al*.[51]

Depending on the type of ligand used and where the C-H activation takes place, five or six-membered palladacycles could form. The type of carbon (aromatic, (sp^2) or aliphatic, (sp^3 or sp^2)) also has an effect on palladacycle formation. Murahashi *et al.* synthesized N-(2-methylbenzylidene)aniline from 2-methylbenzylaldehyde and aniline, and treated it with $Pd(OAc)_2$ followed by sodium chloride to give exclusively a five-membered chloride-bridged palladacycle via an aromatic C(sp^2)-H activation in excellent yield (95%), as shown in Scheme

1.14.[52] A six-membered palladacycle, which could have formed through C(sp^3)-H activation, was not obtained.



29, 95%

Scheme 1.14. Synthesis of five-membered palladacycle by Murahashi *et al.*[52]

Albert *et al*. investigated the reaction of an imine, 2,4,6-$(CH_3)_3C_6H_2CH{=}NCH_2C_6H_5$, initially with $Pd(OAc)_2$ and subsequently with LiBr, to get a bromide-bridged palladacycle (Scheme 1.15).[53] Interestingly, there are two possible ring sizes, (*endo*- ring A or *exo*- ring B) and two Pd-C bonds (through an sp^2 or sp^3 carbon) that could form (Figure 1.7). A six-membered *endo*-palladacycle, i.e. when the imine double bond is part of the ring, could form if the metallated carbon is sp^3-hybridized (ring A). In contrast, a five-membered *exo*-palladacycle could form through activation of an aromatic sp^2 carbon (ring B). A six-membered *endo*-complex **30** was obtained in good yield (70%) which was the first example of metallation taking place on an aliphatic sp^3 carbon in preference to an aromatic sp^2 carbon (Scheme 1.15).

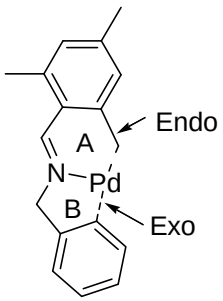
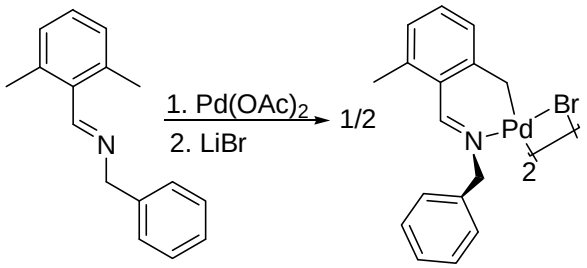


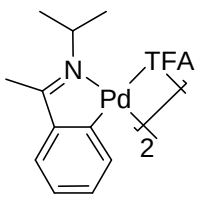
Figure 1.7. *Endo*- and *exo*-palladacycles



31, 70%

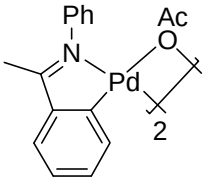
Scheme 1.15. Six-membered palladacycle through a C(sp^3) carbon by Albert *et al.*[53]

Other imine-based palladacycles have been synthesized and tested as pre-catalysts in C-C coupling reactions. In 1999, Milstein *et al*. were the first to report the use of imine-based palladacycles for catalysis in the Suzuki and Heck cross-coupling reactions.[54] Milstein's palladacyclic complex **32** (Figure 1.8) gave TON of 8.4 x10^5 in the Suzuki coupling reaction of activated *p*-acetyl-bromobezene and phenylboronic acid. With deactivated substrates such as *p*-methoxy-bromobenzene, complex **32** gave TONs on the order of 1 x 10^5. All reactions were conducted at 130 ^oC under air as well as under N_2 atmosphere.

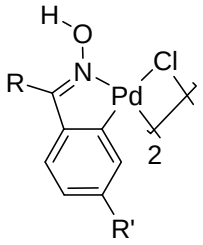


32

TFA = Triflouroacetate



33



34a: R = H, R' = Ph

34b: R = H, R' = Me

34c: R = Cl, R' = *p*-ClC_6H_4

34d: R = OMe, R' = *p*-$MeOC_6H_4$

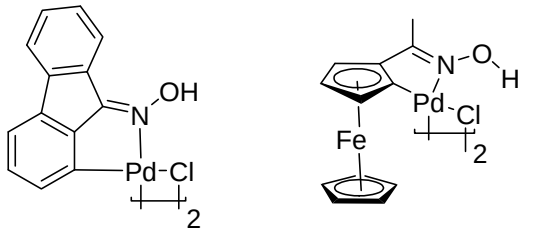
34e: R = Me, R' = OH

34f: R = *p*-C_6H_4OH, R' = OH

Figure 1.8. Five-membered imine-based palladacycles

In further studies, complex **32** was found to be active in the Heck coupling reactions of iodobenzene and bromobenzene with methylacrylate giving TONs of up to 10^6 and 10^4, respectively. In both reactions (Suzuki and Heck) little or no activity with aryl chlorides was observed. Even the modified Milstein complex, **33** (Figure 1.8) did not show any activity with aryl chlorides. However, oxime derived complexes (**34a-34f**) synthesized by Nájera *et al.* were effective in coupling of activated and deactivated aryl chlorides for the Suzuki coupling reaction.[55] These precatalysts were described to be soluble in water due to the oxime functionality; consequently, coupling reactions were performed under aerobic conditions to obtain TONs of up to 4.7 x 10^3 and TOF of up to 4.7 x 10^3 h^{-1} for activated aryl chloride substrates. Although deactivated substrates, for instance *p*-methoxychlorobenzene, even in the presence of Bu_4NBr gave lower activity (TON of 80 and TOF of 13 h^{-1}). In another study, Iyer *et al.*[56] employed oxime-based palladacyclic complexes (R = H, R′ = H (**35**) and R = H, R′ = Ph (**36**)) similar to Nájera's catalysts (**34a-34f**) above. Complex **35** gave a TON of 300 in the Heck coupling reaction of highly activated *p*-nitrochlorobenzene with ethyl acrylate. However, when deactivated aryl halide substrates (e.g. *p*-methylchlorobenzene) were used, drastic reduction in activity was observed (TON = 1). This is much lower than the activities observed in complexes

34a-34f. Another oxime-based complex that Milstein *et al*.[55] studied was a flourenone-based complex **37** (Figure 1.9) which gave a low TON of 199 in the reaction *p*-acetyl-bromobenzene with methylacrylate and 970 with phenylboronic acid. No catalytic activity studies with aryl chlorides were conducted.

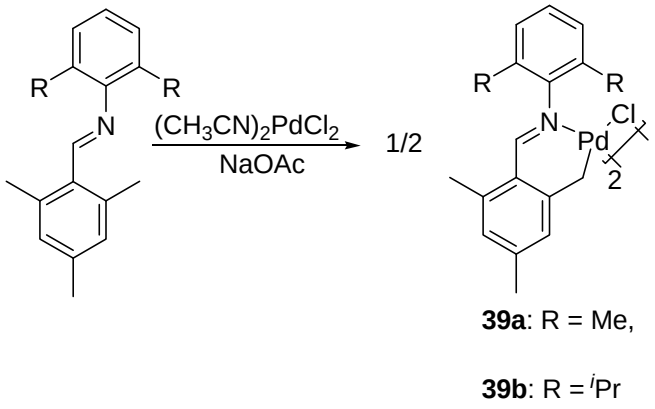


37 **38**

Figure 1.9. Five-membered palladacycles for C-C coupling reactions

An oxime-based catalyst precusor built from acetylferrocence **38** (Figure 1.9) was reported in 1997 by Lopez *et al.*[57] In 2002 it was used in both the Heck and Suzuki coupling reactions by Nájera *et al*.[55] and in 2004 was used only in the Suzuki coupling reaction at different conditions by Iyer *et al*.[58] In the study by Nájera *et al*., complex **38** was tested in reaction of activated *p*-acetylbromobenzene with phenylboronic acid (Suzuki coupling) in toluene at 110 ^{o}C to give a TON of 9.8 x10^4 and TOF of 9.1 x 10^4, whereas the reaction of iodobenzene with methylacrylate (Heck reaction) using triethylamine as the base gave a TON of 9.4 x 10^3, TOF = 1.6 x 10^3 h^{-1}. No activation of aryl bromides or chlorides was reported by Nájera *et al*. Studies by Iyer *et al.*, used Na_2CO_3 as the base instead of triethylamine. They also employed complex **38** in the Heck coupling reaction of a more deactivated substrate, *p*-methoxyiodobenzene, which with ethylacrylate gave a TON of 6.3 x 10^4 and TOF of 5.2 x 10^3 h^{-1}. In addition, reaction of bromobenzene with styrene resulted in TON of 7.0 x 10^4 (TOF = 808 h^{-1}). Surprisingly reduced activities were observed when a more activated substrate, *p*-cyanochlorobenzene (TON = 28, TOF = 1 h^{-1}) was used. These results however are not comparable since different authors used

different reaction conditions and substrates. In 2005, Chen *et al.* in two separate accounts, reported the preparation and application of six-membered palladacycles **39a-39b** in the Suzuki reaction (Scheme 1.16).[59,60] They were found to have good activity (TONs of up to 10^6) for activation of activated aryl bromides such as *p*-acetylbromobenzene with phenylboronic acid under air in ethanol and water. Activity for *p*-methoxybromobenzene, a deactivated aryl bromide, gave decreased TONs of 2 x10^4. When aryl chlorides were employed as substrates, no activity was observed. However, addition of tetra-*n*-butylammonium bromide (TBAB) to the above reaction resulted in an increased activity, giving TONs of up to 8.0 x 10^3.

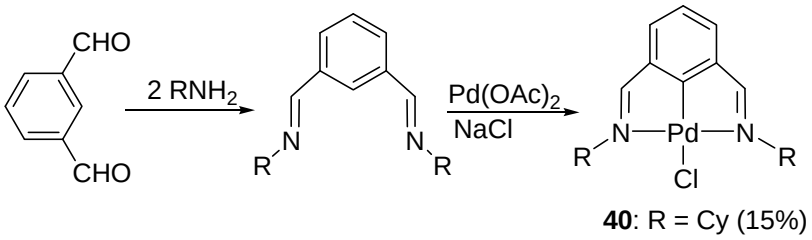


39a: R = Me,

39b: R = ^{i}Pr

Scheme 1.16. Synthesis of a six-membered *endo*-palladacycle through an sp^3 carbon

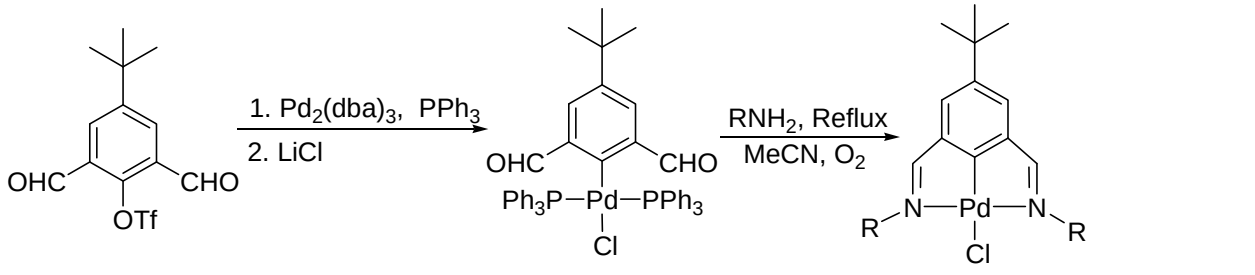
Imine-based pincer [NCN] palladacycles have also been reported in literature using different synthetic routes. Vila *et al*. started with a condensation reaction of isophthalaldehyde with cyclohexylamine to give a 1,3 diimine, 1,3-(CyN=CH)$_2$C$_6$H$_4$, (Scheme 1.17). This was treated with Pd(OAc)$_2$ and then further with NaCl to obtain a chloride-bridged imine-based [NCN] pincer complex **40**, through a direct C-H activation method.[61] No catalytic activity studies with complex **40** were reported.



40: R = Cy (15%)

Scheme 1.17. Synthesis of [PCP] pincer palladacycles[61]

Similar complexes were obtained in higher yields (86-98%) by Takenaka *et al*. in 2005 when a different strategy was employed.[62] The method first involved a site-controlled metallation of an aromatic ring followed by the introduction of the imine functionality as shown in Scheme 1.18. Thus, reaction of dialdehyde, 4-*t*-butyl-2,6-diformylphenyl trifluoromethanesulfonate (**A**) with $Pd_2(dba)_3$ in the presence of triphenylphosphine and LiCl results in complex **B** via oxidative complexation. Complex **B** was reacted with a primary amine in acetonitrile under an O_2 atmosphere to afford complexes, **41a-41e** in excellent yields (86-98%).



A

B (92%)

41a: R = Cy (92%) **41d:** R = Bn (86%)

41b: R = Bu (98%) **41e:** R = ^{t}Bu (96%)

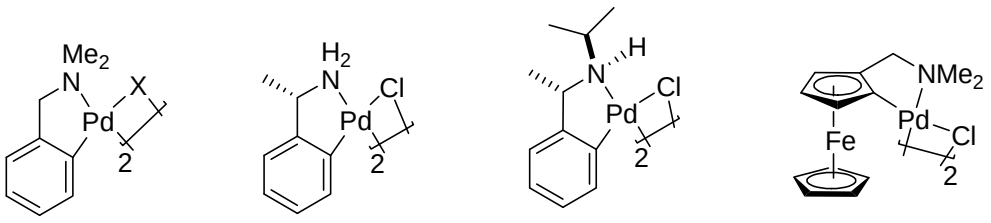
41c: R = Adamantyl (91%)

Scheme 1.18. Synthesis of imine [NCN] pincer palladacycles[62]

Complexes **41a-41e** were tested in the Heck coupling reaction of iodobenzene with methylacrylate, giving TONs ranging from 86 for **41c** and **41e** to 91 for **41b**. Complex **41b** was also employed under optimized conditions for both activated and deactivated iodobenzene with methylacrylate and *n*-butylacrylate giving TONs of up to 9.1 x 10^5 (TOF of 1.9 x 10^4 h^{-1}) in the presence of TBAB and water.[62]

1.3.2 Amine-based [CN] and [NCN] Palladacycles and Catalysis

Five-membered amine-based [CN] palladacycles have also been synthesized using primary, secondary and tertiary amines and are reported in the literature (Figure 1.10).[63, 64] In 1968, Cope *et al.* reported the synthesis of complex **42a** in 95% yield by treating N,N-dimethylbenzylamine with Li_2PdCl_4.[65] Subsequently, a number of different variations in the ligand motif have been synthesized. In 1993, Vicente *et al*. reported the first example of an optically active palladacycle **43** using a chiral primary amine as a starting material through *ortho*-palladation.[66] Complex **44**, using a secondary amine, was synthesized by Dunina *et al*. in 1995 and was used in enantiomeric discrimination of racemic *tert*-butylmethylphenylphosphine.[67] In this section, however, emphasis will be placed on fully characterized complexes that have found applications in C-C coupling reactions. Interestingly, complex **42a** was employed by four research groups for C-C coupling reactions. In 1998, Bedford *et al*. used it as a pre-catalyst in the Suzuki reaction between an activated aryl bromide and *n*-butyl acrylate to give a TON of 265.[27]



42a: X = Cl

42b: X = TFA

43

R_CS_N - **44**

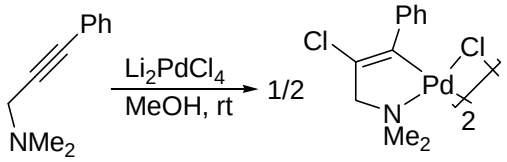
45

Figure 1.10. Five-membered amine-based palladacycles

In 2000, Iyer *et al*. tested the aforementioned complex **42a** in the Heck coupling reaction. TONs of up to 9.0 x 10^4 and 8.6 x 10^4 were obtained when phenylbromide was reacted with ethylacrylate and styrene, respectively. When an activated chloride (*p*-nitrochlorobenzene) was treated with ethyl acrylate, lower activities (TON of 287) were observed. With styrene, however, higher activities were recorded (TON of 7.0 x 10^4).[56] In 2001, using complex **42a**, Beletskaya *et al*. conducted the same reaction at different conditions and obtained very low activities of up to 10^3 TONs.[50] Furthermore, Yang *et al*. employed complex **44** and reported high activities (up to 3 x 10^6 TONs) when iodobenzene was reacted with methylacrylate instead of ethyl acrylate.[68] Although, when deactivated aryl iodides were employed, activities drastically reduced TONs to 9.0 x 10^4 at best. TONs of less than 10^3 were recorded for activation of aryl bromides using substrate:catalyst mole ratio of 1000:1. No activities were reported for activation of aryl chlorides. An amine-based palladacycle **45** built on a ferrocence scaffold was also used by Yang *et al*. and gave a TON of 3 x 10^6 when reacting iodobenzene with methyl acrylate, while no activity with bromobenzene was observed.[68]

Palladacycle **46** was initially synthesized by Yukawa *et al*. in 1968 in almost quantitative yield from the reaction of Li_2PdCl_4 with 3-(dimethylamino)-1-phenyl-1-propyne (Scheme 1.19).[69] **46** was later employed by Consorti *et al*. in the Heck coupling reaction of aryl halides

with olefins even at room temperature.[70] The complex demonstrated activity towards activation of electron rich *p*-methoxyiodobenezene and electron deficient *p*-nitrobromobenzene with *n*-butylacrylate at room temperature giving TONs of 400 and 80, respectively. Activation of aryl chlorides was observed at room temperature, but increasing the temperature to 150 ^{o}C gave TONs of up to 10^3 for activated aryl chlorides. No activity with deactivated aryl chlorides was observed. Nonetheless, it is noteworthy that it is very rare to find Heck reactions that are performed at room temperature using palladacyclic complexes.



46

Scheme 1.19. Synthesis of amine [CN] palladacycles[69]

Six-membered amine-based palladacyclic complexes have also been reported in the literature. In 1996, Albert *et al*. reported on cyclometallation of a primary amine, 2-phenylaniline, to obtain a six-membered bromide-bridged dinuclear complex (**47**) in 49% yield (Figure 1.11).[71] In 2005, chloride- and acetate-bridged complexes analogous to **47** were later obtained by the same research group in good yields of 75 and 85%, respectively.[72] In a report that appeared in 1989 by Dupont *et al*., a chloride-bridged palladacyclic complex (**48**) was synthesized using a tertiary amine, N,N-2-(dimethyl)-biphenylamine.[73] To further confirm that six-membered palladacycles can be formed from primary amines in a general synthesis, which was initially thought not to be possible, Vicente *et al*. reported the synthesis of a series of complexes **49a-49d** based on (2-

phenylethyl)amine and its substituted counterparts in good yields.[74, 75] None of these dinuclear palladacycles have been applied in carbon-carbon coupling reactions.

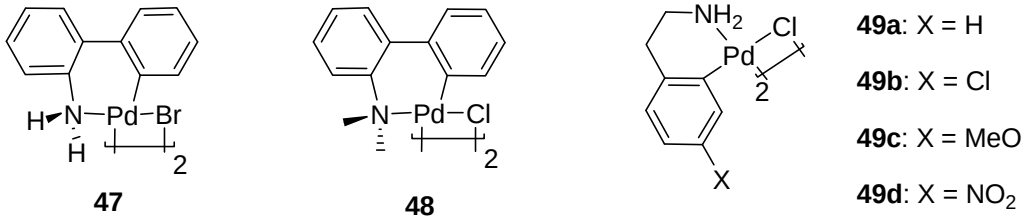
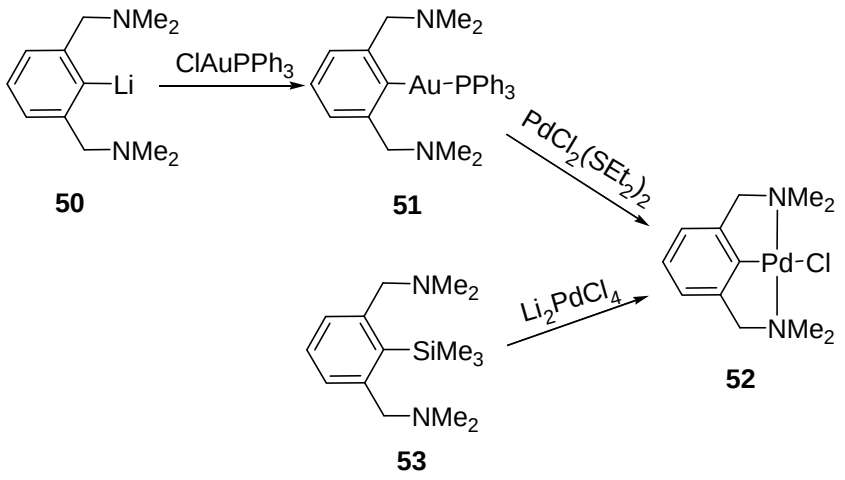


Figure 1.11. Examples of amine [CN] palladacycles

Only a small number of reports on [NCN] amine-based pincer palladacycles exist in the literature, partly due to instability of the donor amine ligands. Two representative synthetic protocols for the synthesis of **52** are presented in Scheme 1.20. Contel *et al*. reported a novel synthesis in which a lithiated ligand, [Li(NCN)] **50** was reacted with $AuCl(PPh_3)$ to obtain $AuPPh_3(NCN)$ complex **51** in good (68%) to excellent yield (quantitative). Transmetallation reaction of complex **51** with $PdCl_2(SEt_2)_2$ gave the desired compound **52** in 96% yield.[76] Compound **52** was also obtained by Steenwinkel *et al*. in 95% yield from the reaction of a silylated ligand **53** with Li_2PdCl_4 (Scheme 1.20).[77]



Scheme 1.20. Synthesis of amine [NCN] pincer palladacycles[77]

No record of C-C coupling reactions using complex **52** or any other pincer NCN amine-based palladacycles exists in the literature.

1.3.3 [CN] palladacycles-whose N donor atom is already part of a ring system

This subsection focuses on the synthesis and applications in the C-C coupling reactions of both five- and six-membered dinuclear [CN] palladacycles whose N donor atom is part of the ring system. These include pyridines, oxazolines, pyrazoles and benzothiazoles. Catalytic studies of complexes **54**, **55** and **56** (Figure 1.12) were carried out by Beletskaya *et al*. in 2001 and showed catalytic activity not only with iodobenzene activation but also with bromobenzene.[50] However, in the activation of iodobenzene in the presence of ethyl acrylate, complex **54** proved to be the most active (followed by complex **56**) giving TONs of up to 4.1 x 10^6 and TOFs up to 5.3 x 10^5 h^{-1}. This compares very well even with the Herrmann's catalyst **3a** in a similar reaction. In the reaction of bromobenzene and ethylacrylate, complex **54** was barely active as only 3% conversion was recorded. However, under Jeffery conditions, activities increased to a TON of 380. It is also

worth mentioning that in the presence of **56** and without applying Jeffery conditions, activated bromobenzene (*p*-acetylbromobenzene) reacted with ethyl acrylate and styrene to give TONs of 4.4 x 10^5 and 10^3, respectively.

Nonoyama reported the syntheses of a series of six-membered palladacycles based on **57** from a reaction of 2-aminopyridine derivatives with $PdCl_2$ (Figure 1.12).[78] Optically active five-membered palladacycle **59**, with a Pd-C(sp^3) bond, was first synthesized in 1972 by Sokolov *et al*. through direct metallation into a methylene group.[79] Six-membered palladacycle **58** obtained from the reaction of benzyl pyridine was reported by Hiraki *et al*.[80] No catalytic studies were carried out using complexes of type **57-59**. Five-membered oxazoline-based palladacycle **60** reported by Manuela *et al.* and was found to be active in the Heck arylation of olefins with iodobenzene and bromobenzene giving TONs of 1.42 x 10^5 and 1.32 x 10^5, respectively.[81]

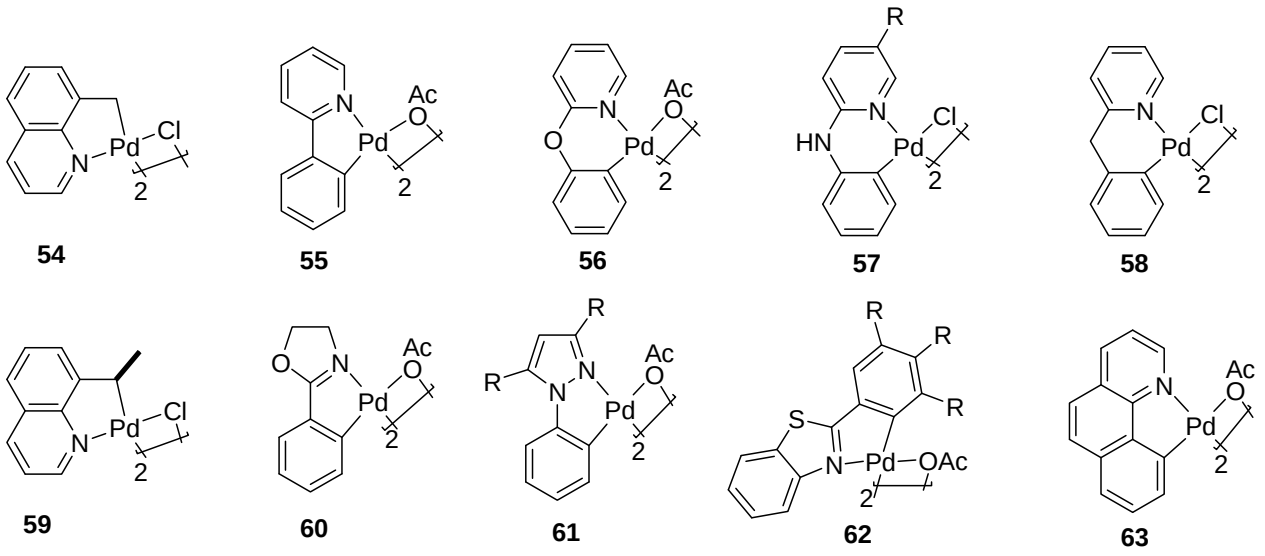


Figure 1.12. Different types of [CN] palladacycles in which the N atom is part of a ring system

In 2000, Gai *et al*. reported five-membered pyrazole- and benzothiazole-based palladacycles (**61** and **62**, respectively) as efficient catalysts for Heck coupling reactions of iodobenzene and *n*-butyl acrylate under slightly mild conditions (90-100 ^{o}C). The reported TONs ranged from 1.48 x 10^6 to 2 x 10^6 for pyrazole-based and 9.8 x 10^4 to 1.0 x 10^5 for benzothiazole-based palladacycles.[82] Complex **63**, a benzoquinoline-based palladacycle, had no record of C-C coupling reaction studies.[83]

Pincer [NCN] palladacycles in which the N-donor atom is part of a ring have also been reported (Figure 1.13). Complex **64** with five-membered fused metallacycles was tested in the reaction of aryl iodides with methylacrylate using a microwave oven. TONs and TOFs of up to 9.3 x 10^4 and 2.8 x 10^4 h^{-1}, respectively, were recorded. In the absence of microwave energy, they reported decreased activities of 7.5 x 10^4 (TON) and 5.4 x 10^3 h^{-1} (TOF).[84]

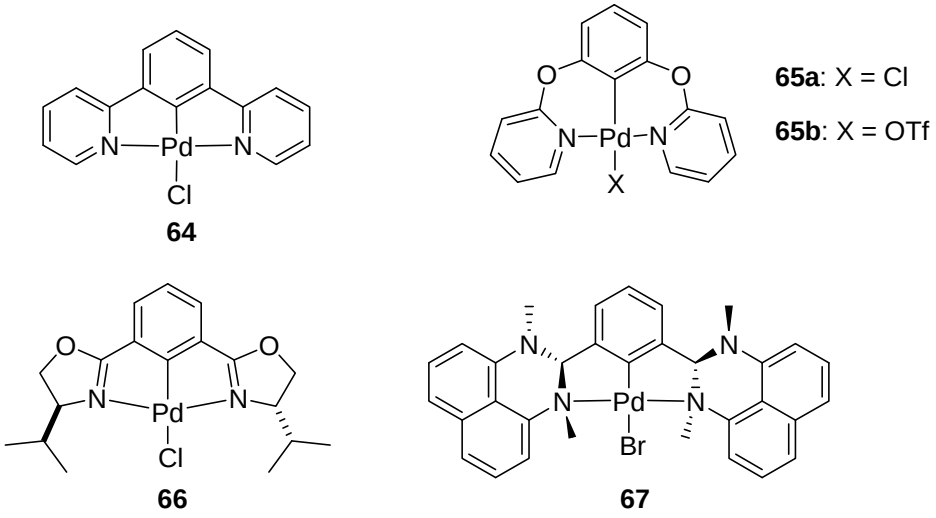


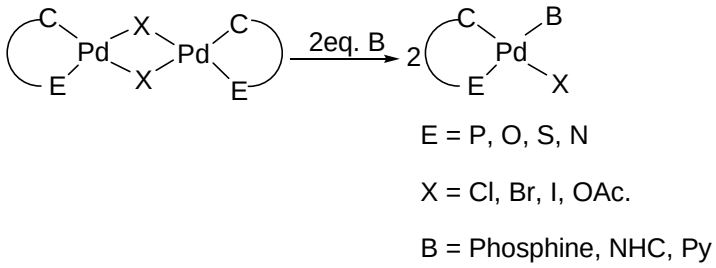
Figure 1.13. Examples of [NCN] palladacycles

In 2006, Yoon *et al*. synthesized pincer complexes composed of six-membered fused palladacycles. Chloropalladium complex **65a** was attained in 80% yield from direct reaction of

1,3-bis(2-pyridyloxy)benzene and K_2PdCl_4. While its triflate analogue, complex **65b** was obtained from further reaction of chloropalladium complex **65a** with silver triflate.[85] Both complexes were found to be active in C-C coupling reactions. However, **65a** was reported to be less active than **65b**. For instance, complex **65a** gave TONs of up to 4.3×10^6 in the coupling of iodobenzene and methyl acrylate, while complex **65b** gave 8.5×10^6 for the same reaction and under the same reaction conditions. No activities were observed when coupling aryl bromides using complex **65a**, but complex **65b** gave TONs of up to 5.0×10^3. Both complexes were inactive towards activation of aryl chlorides. Complex **66** was found to be active in the activation of aryl iodides and phenylboronic acid (Suzuki reaction) giving TONs of up to 9.0×10^5 and TOFs of up to 4.5×10^4 h^{-1}. In 2003, Jung *et al.* synthesized a Pd-NCN pincer complex (**67)** and it was found to be an active pre-catalyst towards the Heck coupling reaction of aryl iodides with methyl acrylate, giving TONs of 4.3×10^6. When deactivated bromobenzene and chlorobenzene were used as substrates no activity was observed.[86]

1.4 Mononuclear Palladacycles and Catalysis

Mononuclear palladacycles are obtained in good yields by reacting halide- or acetate-bridged dinuclear palladacycles with phosphines, *N*-heterocyclic carbenes (NHC) or pyridine-based compounds as shown in Scheme 1.21. Some catalytic activity studies of mononuclear palladacycles show that they are more active than their dinuclear counterparts, as will be shown below.



Scheme 1.21. General synthesis of mononuclear palladacycles from dinuclear palladacycles

1.4.1 Phosphine-adduct Palladacycles

The use of phosphine-based compounds to split dinuclear palladacyclic complexes has been known since the 1970s.[87] However, the resultant mononuclear species were not applied in carbon-carbon coupling reactions until 2001 when Bedford *et al.* tested complexes **68** and **69** (Figure 1.14) in the Suzuki coupling reaction.[88] Both were found to be efficient precatalysts in the coupling of both deactivated and activated aryl chlorides with phenylboronic acid. Using a deactivated substrate (*p*-methoxychlorobenzene), complex **68** and **69** gave TONs of up to 2.6 x 10^3 and 8.0 x 10^3 (reaction conducted under air). These results clearly showed complex **69** to be superior catalyst to **68**. Higher activities (TON = 9.9 x 10^4) were observed when an activated substrate, *p*-acetylchlorobenzene, was coupled with phenylboronic acid in the presence of **69**. It is worth noting that complex **69** shows the highest activity reported in the coupling of either electron withdrawing or electron donating aryl chlorides of all palladacyclic complexes. Additionally, both mononuclear species were more active than their corresponding dinuclear palladacycles (**32** and **42b)**. Amine-based palladacycles **70** and ferrocenylamine-based palladacycle **71** synthesized by Yang *et al.,* were found to be effective in the Heck coupling reaction of iodobenzene with methylacrylate giving high TONs of up to 9.1 x 10^6 and 9.6 x 10^6, respectively. These activities show a threefold increase, for the same coupling reaction under the same reaction conditions,

compared to their corresponding dinuclear compounds **42a** and **45**. In the activation of aryl bromides, no activities were observed when either mononuclear species (**70** and **71**) or their dinuclear counterparts **42a** and **45** were employed as precatalysts.[68]

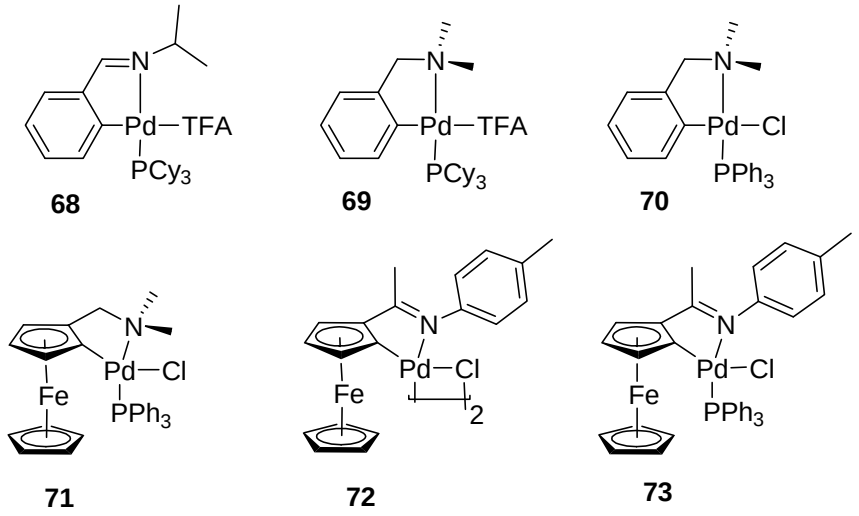


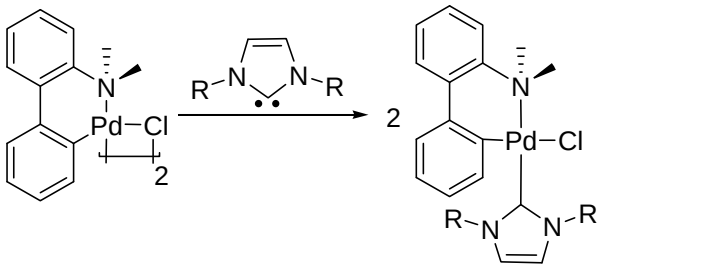
Figure 1.14. Examples of five-membered amine and imine [NC] palladacycles

Chloride-bridged ferrocenylimine-based palladacycle **72** and its related mononuclear phosphine-ligated palladacycle (**73**) were reported by Yang *et al.* as efficient precatalysts in the Sonogashira cross-coupling of aryl halides with terminal alkynes. Yet again, this report exemplifies that mononuclear palladacycle **73** shows superior activity over dinuclear palladacycle **72**.[89]

1.4.2 *N*-Heterocyclic Carbene-adduct Palladacycles

As observed in Chapter 1.4.1, phosphine-based compounds have been successfully applied as bridge splitting ligands, however many researchers are working towards replacement of phosphines due to difficulties in removing decomposed phosphine by-products, expensive bulky tertiary phosphines and limited choice of phosphine starting materials. *N*-Heterocyclic carbenes

(NHCs) have therefore been considered as alternatives to phosphines due to their higher σ-donating ability and wide selection of starting materials.[90] In 2003, Nolan *et al*. reported the synthesis of mononuclear NHC-based palladacycles that were obtained from the reaction of amine-based palladacycles and free NHCs as shown in Scheme 1.22.[91] In another report by the same authors, the complexes were tested and found active in the Suzuki coupling reaction of a series of aryl chlorides with phenylboronic acid. Thus, using 2 mol % loading of precatalysts **74a** and **74b**, both deactivated (e.g. *p*-methoxychlorobenzene) and activated (e.g. *p*-acetylchlorobenzene) aryl chlorides were coupled with phenylboronic acid giving TONs of up to 43 and 48, respectively. Additionally, sterically demanding deactivated aryl chlorides and sterically demanding phenylboronic acid were coupled (TON = 43). Interestingly, all reactions were conducted at room temperature using 2-propanol as the solvent, making the process eco-friendly and less expensive.[92, 93]



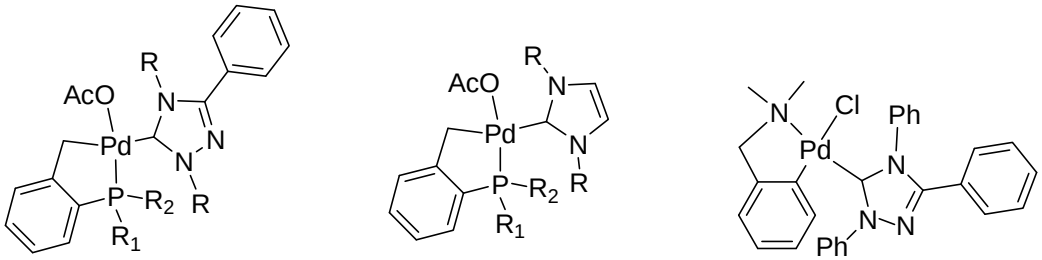
74a: R = 2,6-$^{i}Pr_2$-C_6H_3

74b: R = 2,4,6-Me_3-C_6H_2

Scheme 1.22. Synthesis of NHC-adduct palladacycles[91]

In 2005, using the method as outlined above (Scheme 1.22), Herrmann *et al*. synthesized a series of NHCs containing phospha- and amine-palladacycles.[94] Representative compounds are shown in Figure 1.15. These compounds were reported to be active for the Heck coupling reaction of

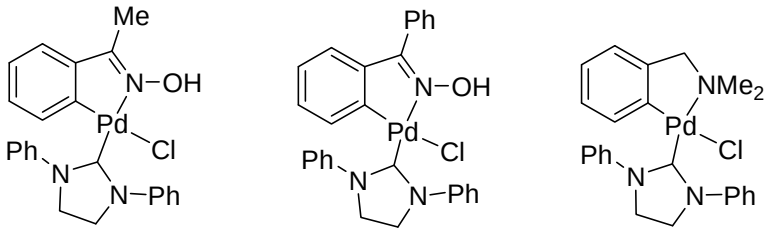
aryl halides and styrene under Jeffery conditions. Among the three complexes, palladacycle **77** gave the highest activity (TON = 5.0 x 10^5) followed by **75** with a TON of 3.4 x 10^5, and palladacycle **76** gave TONs of up to 1.1 x 10^5 when an activated aryl bromide (*p*-acetylbromobenzene) and styrene were employed. Activation of an aryl chloride with electron withdrawing groups (*p*-acetylchlorobenzene) and styrene was also achieved, although low yields were obtained.



75: R = Ph, R_1 = R_2 = *o*-tol **76**: R = Mes, R_1 = *o*-tol, R_2 = ^{t}Bu **77**

Figure 1.15. Examples of NHC-adduct [NC] and [PC] palladacycles by Herrmann *et al.*[94]

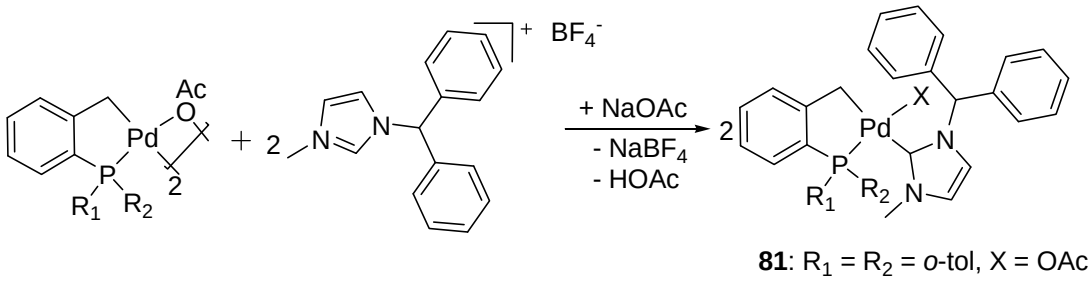
In 2003, along the same lines as above, Iyer *et al.* synthesized NHC-adducts of *ortho*-palladated aryl oximes (**78-79**) and amines (**80**) (Figure 1.16). These complexes showed an increased thermal stability and the ability to catalyze the Heck and Suzuki coupling reactions of aryl bromides with moderate to high TON (2.0 x 10^3 and 9.2 x 10^4) and TOF (200 and 4.3 x 10^3 h^{-1}), respectively. Coupling with aryl chlorides was observed, albeit with less success.[95]



78 **79** **80**

Figure 1.16. NHC-adduct of imine and amine [NC] palladacycles[95]

In 2006 Herrmann *et al*. reported an alternative synthesis to NHC-containing palladacycles in a one-pot synthesis. Instead of generating a free NHC then treating it with a halide- or an acetate-bridged dinuclear palladacycle, phospha-palladacycles were reacted directly with an imidazolium salt in the presence of sodium acetate as shown in Scheme 1.23.[96] It was also reported that only acetate-bridging phospha-palladacycles and imidazolium salts in the company of weak coordinating counterions such as BF_4^- and PF_6^- gave the desired product. Halide counterions resulted in ligand exchange giving halide-bridging dinuclear palladacycles instead of mononuclear NHC-adduct palladacycle (**81**).

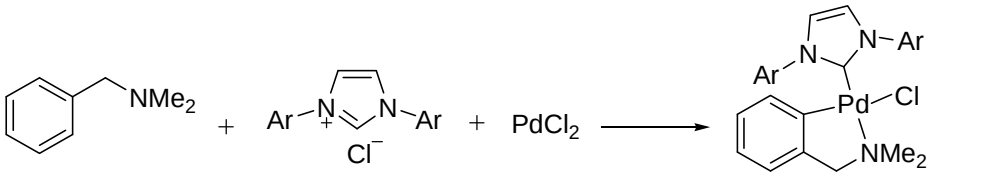


81: $R_1 = R_2$ = *o*-tol, X = OAc

Scheme 1.23. Synthesis of bulky NHC-adduct palladacycles by Herrmann *et al*.[96]

In 2008, Kantchev *et al.* used a novel one-pot, three-component reaction to synthesize an amine-based NHC palladacycle (**82**) in 90% yield as shown in Scheme 1.24.[97] Complex **82** was tested

and found to be active in the Heck coupling reaction of a wide range of challenging aryl bromide substrates. TONs of up to 5.2 x 10^5 were obtained when a deactivated aryl bromide, *p*-methoxybromobenzene, was coupled with *t*-butylacrylate. However a higher catalyst loading of 2 mol % was required when sterically hindered substrates such as 2,4,6-triispropylphenylbromide were coupled with *t*-butylacrylate giving a TON of 36. Activation of aryl chlorides was not reported.

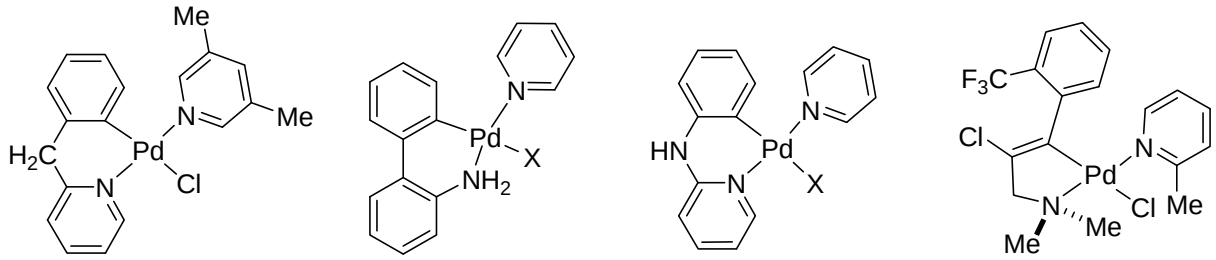


82: Ar = 2,4,6-Me_3-C_6H_2

Scheme 1.24. One pot three-component synthesis of an NHC-adduct palladacycle[97]

1.4.3 Pyridine-adducts of Five- and Six-membered Palladacycles

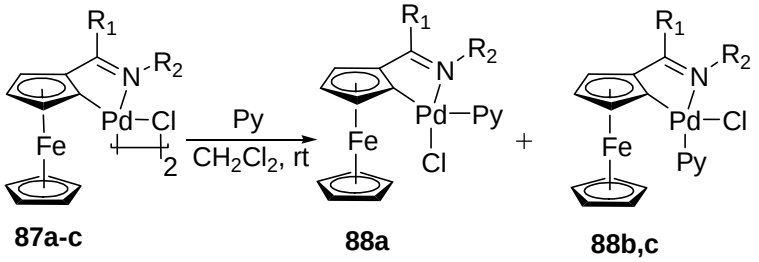
In 1981, pyridine adducts of six-membered palladacycle **83** (Figure 1.17) were synthesized by Hiraki *et al*. in good yield through treating its corresponding chloride-bridged dinuclear complex with 2 equiv of 3,5-dimethylpyridine.[80]



83 **84a**: X = Cl **84b**: X = I **85a**: X = Cl **85b**: X = I **86**

Figure 1.17. Examples of pyridine-adduct palladacycles

Other five- and six-membered mononuclear palladacycles have also been achieved by employing pyridine and pyridine-based compounds. Representative structures **84-86** are shown in Figure 1.17. All mononuclear species adopt a *trans* configuration of the coordinated pyridine with respect to the N-donor atom. However, there is a report by Xu *et al.* on the synthesis of complex **88a** as the only example of a *cis* configuration using a ferrocenylimine palladacycle as shown in Scheme 1.25.[98] Interestingly, the other two complexes, **88b** and **88c** adopt a *trans* configuration. Catalytic activity of all three pyridine-adduct palladacycles towards the Suzuki coupling reaction of deactivated and activated aryl bromides and phenylboronic acid gave TONs of up to 452 and 1.0 x 10^3, respectively. Furthermore, TONs of up to 375 were obtained when a sterically hindered substrate, 2,6-dimethylbromobenzene, was employed.



87a-c **88a** **88b,c**

a: $R_1 = CH_3$, $R_2 = p\text{-}CH_3\text{-}C_6H_4$

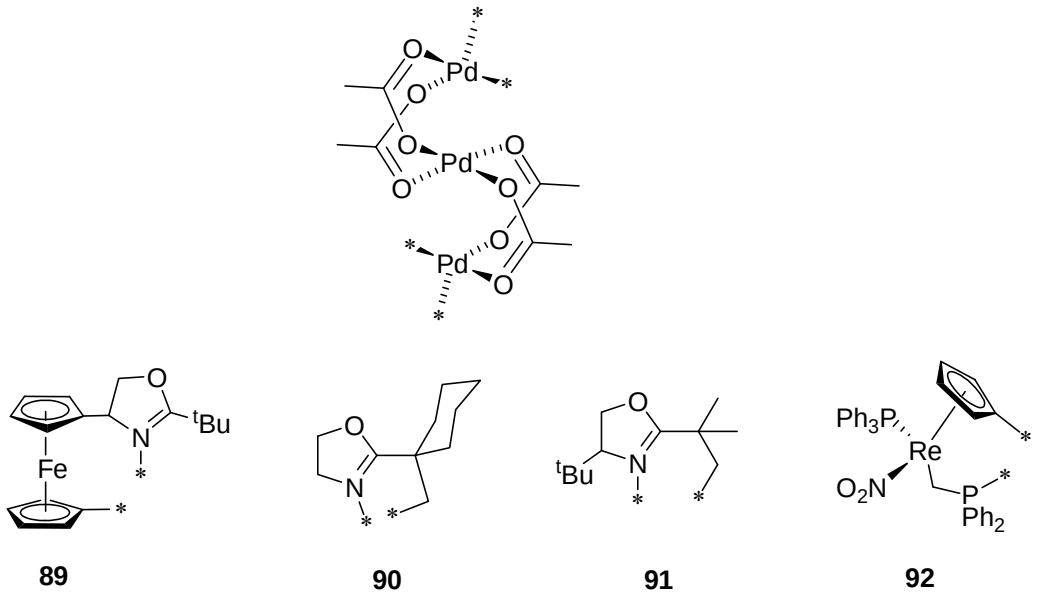
b: $R_1 = CH_3$, $R_2 = p\text{-}Br\text{-}C_6H_4$

c: $R_1 = H$, $R_2 = Cy$

Scheme 1.25. Synthesis of pyridine-adduct of ferrocene-based palladacycles[98]

1.5 Trinuclear Palladacycles

S-shaped trinuclear acetate-bridged palladacycles with a rare $Pd_3(OAc)_4$ core have been published in the literature (Figure 1.18). There are only five reports of such compounds that have been characterized by single-crystal X-ray crystallography. In 2005, Moyano *et al*. reported the synthesis of complex **89** using a 4-ferrocenyl-1,3-oxazoline as the ligand.[99] In the same year, Giri *et al.* investigated the reactivity of oxazoline-based ligands with palladium acetate and obtained trinuclear, C(sp^3)-Pd bonded palladacycles **90** and **91**.[100] Complex **92**, synthesized from a rhenium cyclopentadienyl fragment, was reported by Friedlein *et al.*[101, 102] We explored the reactivity of a γ-diimine ligand with palladium acetate resulting in a trinuclear palladacycle and the details of this investigation will be discussed in Chapter 2.



89 **90** **91** **92**

Figure 1.18. Examples of S-shaped trinuclear palladacyclic complexes

1.6 Diimines as ligands in Palladium and Aluminum Chemistry

Diimine ligands are neutral, chelating 4-electron donors and can be classified as α-diimines (1,2-diimine), β-diimines (1,3-diimines) and γ-diimines (1,4-diimines) as shown in Figure 1.19. The synthesis of diimines typically involves the condensation reaction of either a diketone or a dialdehyde with two equivalents of a primary alkyl or aryl amine. Subsequent reaction of the diimine ligands with a metal precursor (often a metal halide) gives the corresponding metal complex (Scheme 1.26).[103]

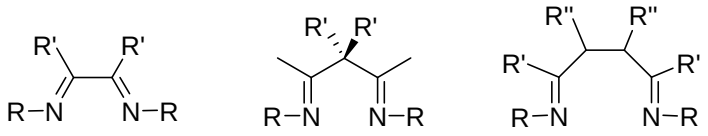
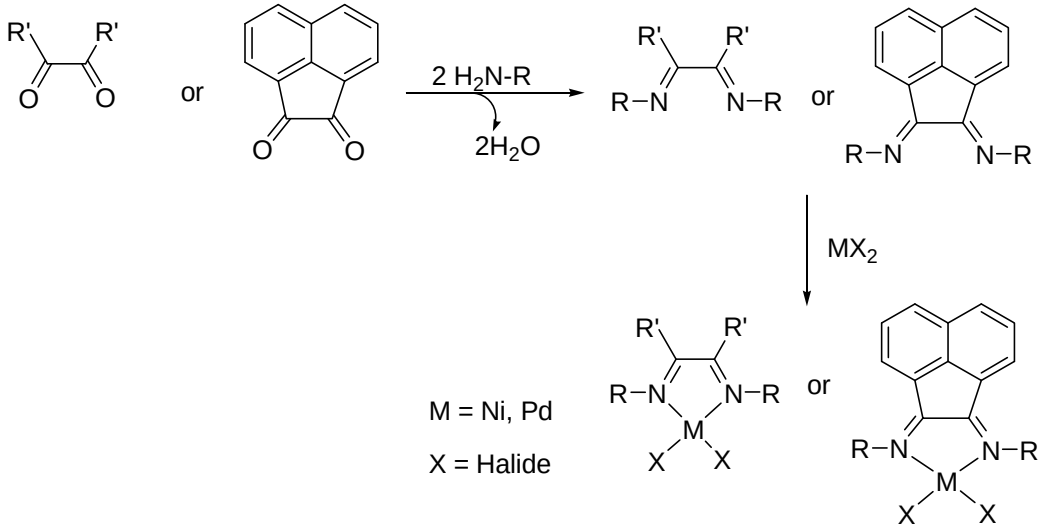


Figure 1.19. Types of diimine ligands

The major advantage of α- and β-diimines is the ease with which steric and electronic properties can be adjusted through the use of various substituents on the amine. Additionally, variations on the ligand backbone also allow the syntheses of a wide variety of ligands and subsequent complexes (Scheme 1.26 and Figure 1.19).



Scheme 1.26. Synthesis of α-diimine ligands and group 10 complexes

1.6.1 α-Diimine ligands and their Applications

α-Diimines based on 1,4-diazabutadienes (DAB)-R or bis(aryl)acenaphthenequinone-diimine (BIAN-R) of the general formula RN=C(R')C(R')=NR have received considerable attention in recent years due to their application as ligands in a wide variety of catalytic reactions. It was initial reports by Brookhart *et al.* in the field of olefin polymerization and olefin/CO copolymerization using Ni(II) and Pd(II) complexes that initiated the widespread interest in applications of these diimines as ligands.[103-109] Group 10 complexes showed higher activities than the classic Ziegler catalysts and exhibited a greatly reduced susceptibility to poisoning by polar

functionalities. Bulky aryl groups such as 2,6-diisopropylphenyl were required to obtain higher molecular weight polymers (Figure 1.20).[104]

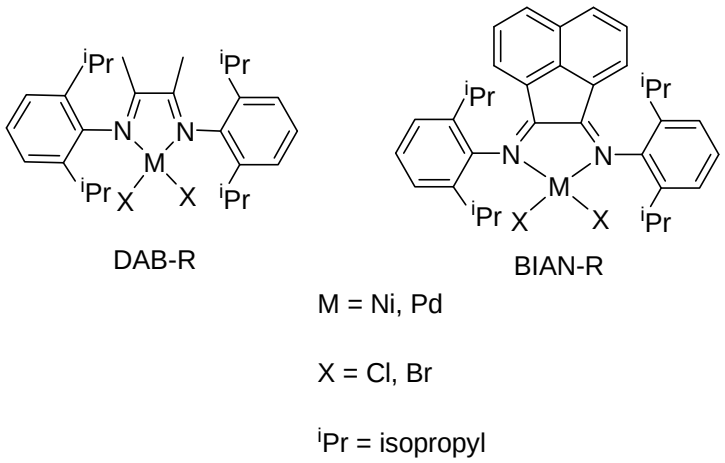
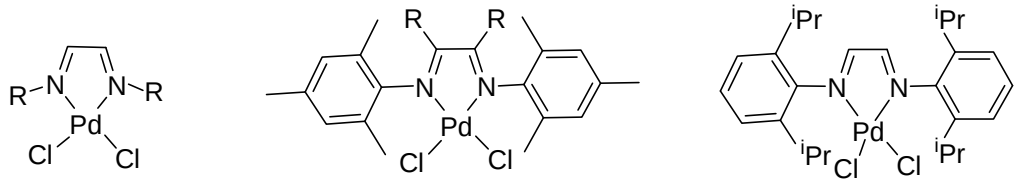


Figure 1.20. Ni(II) and Pd(II) complexes of α-diimine used by Brookhart *et al.* for olefin polymerization[104]

This class of ligand has become increasingly popular due to its ease of synthesis and outstanding steric and electronic tunability. The most common synthetic route to diimine ligands is a simple condensation reaction of primary amines or anilines with diketones or dialdehydes, thereby producing a wide range of α-diimines (Figure 1.19).[103, 110]

Few reports exist in the literature on the application of (α-diimine)Pd(II) complexes as active pre-catalysts for the Suzuki and Heck cross-coupling reactions. Nolan *et al.* reported in-situ preparation of (α-diimine)Pd(II) complexes **93a-93b** for application in Suzuki and Heck C-C coupling reactions (Figure 1.21).[111, 112] Activity largely depended upon a number of factors such as base, additive concentration, solvent, Pd source and the supporting ligands. For instance, complexes **93a** and **93b** containing alkyl substituents on nitrogen atoms gave higher TONs of 31

and 27, respectively, when reacting *p*-methylbromobenzene with *t*-butylacrylate. Complexes with bulky aryl substituents (**94b** and **95)** gave low TONs of about 10. Increased TONs of up to 25 were recorded when complex **94b,** which contains methyl groups in the ligand backbone instead of hydrogen atoms (as in **94a**), was used. The catalyst loading in all these reactions was 3 mol% and no activity with aryl chlorides was reported.



93a: R = Cy

93b: R = *t*-Bu

94a: R = H

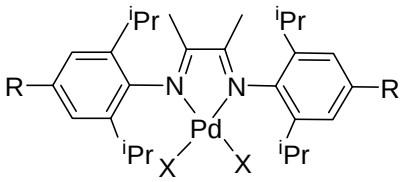
94b: R = Me

95

Figure 1.21. (α-Diimine)Pd(II) complexes used by Nolan *et al.* for Heck coupling reactions [111, 112]

A series of water soluble (α-diimine)Pd(II) complexes were prepared *in-situ* by Zhou *et al.* as active catalyst precursors for the Suzuki coupling reaction. Reactions were carried out with a variety of aryl bromides and arylboronic acids under mild conditions in organic solvents, neat water or a MeOH/H_2O co-solvent mixture (Figure 1.22).[113] Complexes **96a** and **96b** were isolated and showed that coupling reactions could be carried out at room temperature with catalyst loading of 0.01 mol%. Coupling of electron rich aryl bromides (*p*-methoxybromobenzene) and phenylboronic acid (*p*-methylphenylboronic acid) in H_2O was achieved by both complexes **96a** and **96b**. Complex **96a** showed superior activities with a TON of 7.0 x 10^3 compared to 5.7 x 10^3 from complex **96b**. Higher activities (TONs of up to 9.8 x 10^4) were further observed when the reaction was carried out at 70 ^oC in 1:1 H_2O:EtOH solvent mixture using complex **96a**. Electron

deficient aryl chlorides (*p*-nitrochlorobenzene) were also activated, though higher catalyst loading (3.0 mol %) and reaction time (24 h) were required to obtain a TON of 25 using complex **96c**.



96a: R = SO_3Na, X = Cl

96b: R = SO_3Na, X = OAc

96c: R = SO_3Bmim

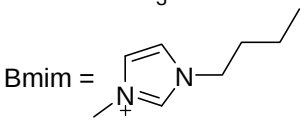
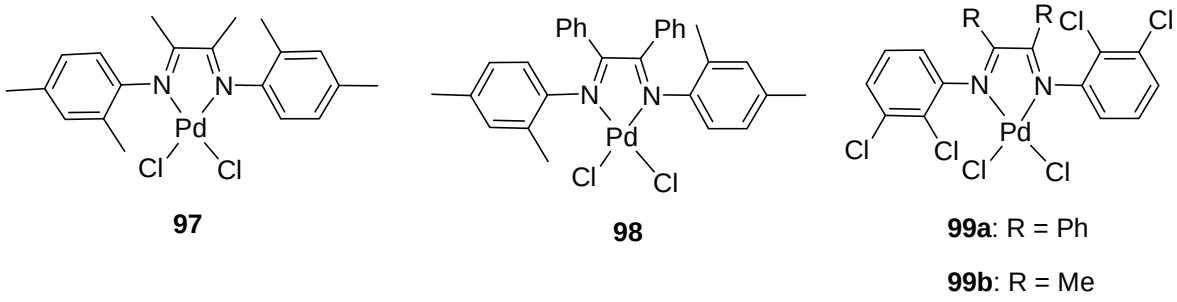


Figure 1.22. (α-Diimine)Pd(II) complexes used by Zhou *et al.* for Heck coupling reactions[113]

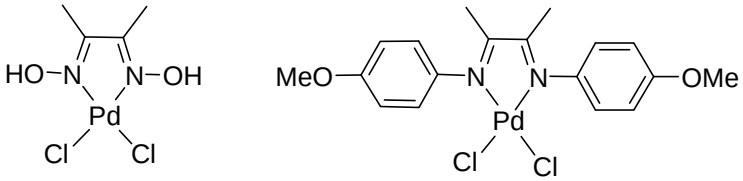
Hanhan's group, in an attempt to investigate the effect of side groups on the ligand towards catalytic activity in C-C coupling reactions, prepared a range of sterically hindered (α-diimine)Pd(II) complexes (Figure 1.23).[114] It was clearly demonstrated that substituting a methyl group with a chloride greatly increased the activity of the complex towards both the Suzuki and Heck coupling reactions. Complex **97** gave low yields (TON = 28) in the coupling of *p*-methyl-bromobenzene with phenylboronic acid, even with higher catalyst loading (3 mol %). Changing the ligand backbone from methyl to phenyl (complex **98**) resulted in a relative increase in yields (TON of up to 59). TONs of 24 and 27 for **99a** and **99b**, respectively, were obtained when methyl groups on the benzene ring were substituted with chloride groups. The same trend was observed in the Heck coupling of *p*-methyl-bromobenzene with methylacrylate; complex **99b** gave the highest TON of 26 while complex **97** gave the lowest TON of 17.



97 **98** **99a**: R = Ph **99b**: R = Me

Figure 1.23. (α-Diimine)Pd(II) complexes used by Hanhan *et al.* for Heck and Suzuki coupling reactions[58, 114]

Another report by Iyer and co-workers utilized (α-diimine)Pd(II) complexes **93a**, **95**, **100** and **101** in the Heck coupling reaction of bromobenzene and ethylacrylate (Figure 1.21, Figure 1.24). Complex **93a** gave the highest yield (TON of 63) followed by **100** and **95** with TONs of 48 and 32, respectively and complex **101** was the least active giving TON of 16. Addition of Bu_4NBr gave slightly improved yields.[58] In all the reports above, little or no activation of aryl chlorides was observed.

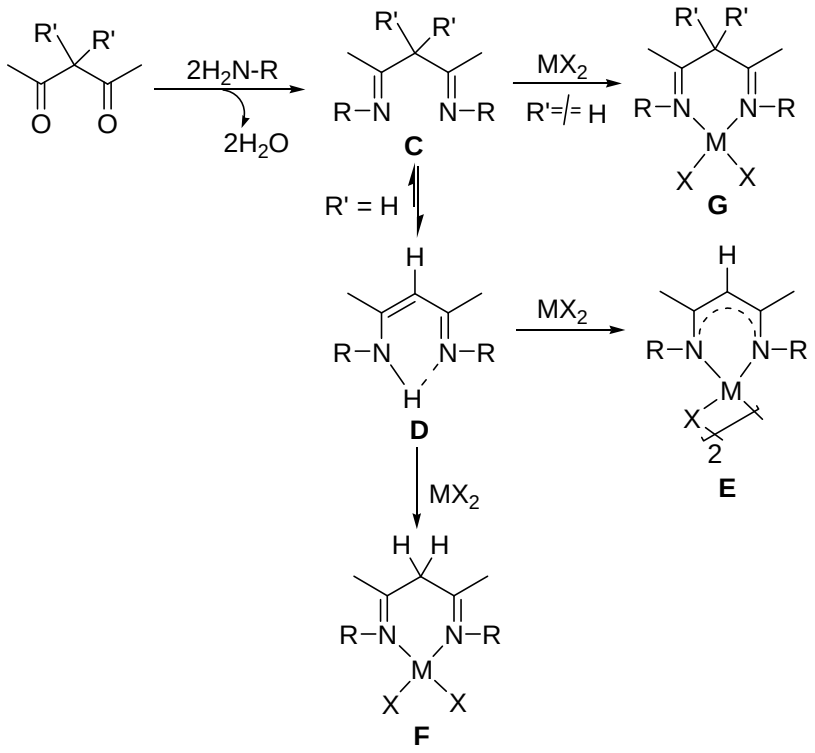


100 **101**

Figure 1.24. (α-Diimine)Pd(II) complexes used by Iyer *et al.* for Heck and Suzuki coupling reactions[58]

1.6.2 β-diimine ligands and their Applications

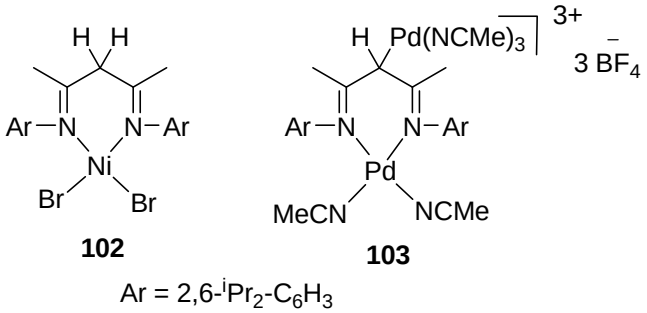
β-diimines (**C**) with CH_2 groups in their backbones readily tautomerize to their enamine isomers and therefore are usually best interpreted as β-diketimines (**D**) (Scheme 1.27). In the presence of a base, deprotonation usually takes place resulting in monoanionic β-diketiminato complexes (**E**) instead of neutral β-diimine complexes (**F**).[115]



Scheme 1.27. General syntheses of β-diimine and β-diketimine ligands and their corresponding complexes

However, there are some examples of neutral β-diimine ligands coordinated to nickel despite having acidic methylene protons on the ligand backbone. β-Diketimines were first coordinated to Ni(II) by Parks *et al.* in 1968 and about 3 decades later Feldmen *et al.* synthesized Ni(II) and Pd(II) complexes using more sterically hindered substrates on the nitrogen atoms (Figure 1.25).[116, 117] Thus, treating the neutral ligand with (DME)$NiBr_2$ resulted in formation of a

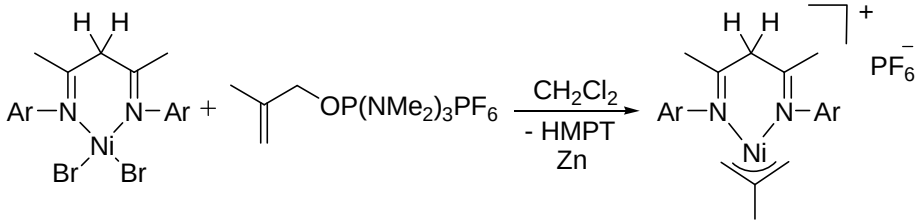
proper neutral (β-diimine)$NiBr_2$ complex (**102**). On the other hand, reaction with $[(MeCN)_4Pd](BF_4)_2$ gives an unusual complex in which one equivalent of $[(MeCN)_4Pd](BF_4)_2$ forms a C_β-palladium bond, while the other equivalent coordinates through the two imine nitrogens to form six-membered complex **103**.



102 **103**

Figure 1.25. Ni(II) and Pd(II) complexes using β-diimine ligands[117]

There are also two reports on syntheses of cationic methallyl Ni and Pd complexes supported by neutral β-diimine ligands by Bouachir *et al.*[118, 119] In 2002, a series of (β-diimine)$NiBr_2$ complexes of type **F** were reported (Scheme 1.28). These complexes were reduced by zinc in the presence of 2-methylallyloxyphosphonium hexafluorophosphate, ($[CH_2=C(Me)CH_2\text{-}O\text{-}P(NMe_2)_3]^+[PF_6]^-$) to obtain the first examples of room temperature stable cationic mononuclear allyl Ni(II) species (**104a-104d**). Yields ranged from 70 to 83% and the complexes were generally found to be excellent catalysts for the oligomerization of styrene, with selectivity of about 98% towards 1,3-diphenylbut-1-ene.



HMPT = Hexamethylphosphotriamide

104a: Ar = C_6H_5

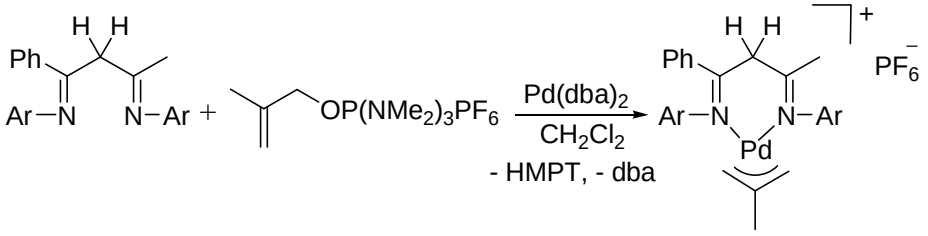
104b: Ar = *o*-CH_3-C_6H_4

104c: Ar = 2,4,6-$(CH_3)_3$-C_6H_2

104d: Ar = 2,6-$^{i}Pr_2$-C_6H_3

Scheme 1.28. Synthesis of cationic mononuclear allyl Ni(II) complexes supported by symmetrical β-diimine ligands[118]

In 2008, palladium(II) complexes analogous to allyl nickel(II) complexes **104a-104d** were synthesized through a three-component one-step reaction (Scheme 1.29).[119] Thus, asymmetrical β-diimine ligands were mixed with $Pd(dba)_2$ in the presence of 2-methylallyloxyphosphonium salt to obtain complexes **105a-105d** in good yields (87-92%).



dba = dibenzylideneacetone

105a: Ar = *o*-CH_3-C_6H_4

105b: Ar = *o*-CH_3O-C_6H_4

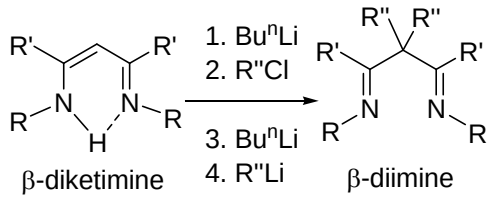
105c: Ar = 2,6-$(CH_3)_2$-C_6H_3

105d: Ar = 2,6-$^{i}Pr_2$-C_6H_3

Scheme 1.29. Synthesis of cationic mononuclear allyl Pd(II) complexes supported by unsymmetrical β-diimine ligands[119]

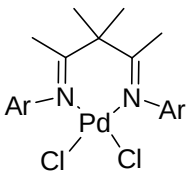
It is worth noting that β-diketimines are very popular ligands and have been successfully employed as monoanionic ligands in a wide variety of reactions to form main group and transition metal complexes.[115] Complexes with group 10 metals in their second (II) oxidation state form halide-bridged dinuclear complexes of type **E** (Scheme 1.27).[120]

To avoid formation of β-diketimines, there are reports in which the acidic methylene protons on the ligand backbone have been substituted by alkyl groups to form neutral β-diimine ligands. Consequently, stable (β-diimine)Ni(II) and (β-diimine)Pd(II) complexes of type **G** (Scheme 1.27), have recently been reported. The first example was synthesized by Woods *et al.* in 2003.[121] Through dialkylation reactions, methylene protons were substituted with methyl groups to formulate a series of neutral diimine ligands; then their activity in reaction with Pd(II) precursors to obtain complexes **106a-106b** were investigated (Scheme 1.30, Figure 1.26).



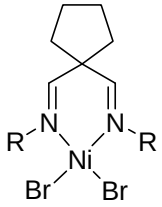
Scheme 1.30. Double alkylation of β-diketimines to form β-diimines[121]

Domin *et al.* reported the syntheses of a wide range of ligands in which the β-carbon is part of a five- or a six-membered ring and were found to be good ligands for preparation of Ni(II) (**107a-107b**) and Pd(II) complexes (**108a-108d**, **109a-109d**) (Figure 1.26).[122, 123]



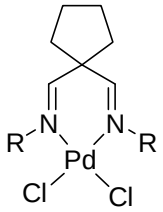
106a: Ar = 2,6-$^{i}Pr_2$-C_6H_3

106b: Ar = 2-^{i}Pr-C_6H_4



107a: R = 2,6-$^{i}Pr_2$-C_6H_3

107b: R = 2,6-Me_2-C_6H_3

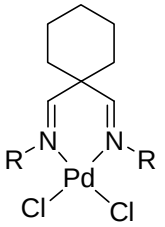


108a: R = 2,6-$^{i}Pr_2$-C_6H_3

108b: R = 2,6-Me_2-C_6H_3

108c: R = Cy

108d: R = ^{t}Bu



109a: R = 2,6-$^{i}Pr_2$-C_6H_3

109b: R = 2,6-Me_2-C_6H_3

109c: R = Cy

109d: R = ^{t}Bu

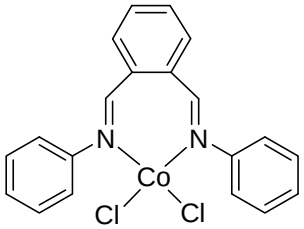
Figure 1.26. β-Diimine Ni(II) and Pd(II) complexes

There has been exploration into the catalytic activity of Ni(II) and Pd(II) complexes containing β-diimine and β-diketimines for olefin polymerization, as well as Suzuki and Heck coupling reactions. A study by Feldman *et al.* showed that (β-diimine)Ni(II) complex **106a** gave reduced activity toward olefin polymerization compared to their α-diimine analogs (Figure 1.20).[117] Zhang *et al.* performed similar studies on a range of (α-diimine)$NiBr_2$ and (β-diketiminato)$NiBr_2$ complexes in which high molecular weight polyethylene and ethylene oligomers were simultaneously produced in the same reaction.[124] Domin *et al.* found Pd(II) complexes **108a-108d** to be active pre-catalysts for the Suzuki coupling reaction of activated and deactivated aryl bromides with phenylboronic acid.[122] Using 3 mol % catalyst loading, TONs ranging from 25 to 33 were recorded. Coupling of activated aryl chlorides (*p*-

acetylchlorobenzene) with phenylboronic acid achieved TON of up to 17. However, no activity was observed when deactivated substrates such as *p*-methoxychlorobenzene were employed. In the Heck coupling reaction of *p*-acetylbromobenzene with methylacrylate, complexes with alkyl substituents on the nitrogen atom (**108c**-**108d** and **109c**-**109d**) gave quantitative yields (33 TON). No activities with chloride-based substrates were recorded. In the Hiyama coupling reactions of deactivated aryl bromides and chlorides with phenyltrimethoxysilane, TONs of up to 29 were recorded.[122] These results, compared to the (α-diimine)Pd(II) complexes, show almost the same activity towards Suzuki and Heck coupling reactions (Section 1.5.1).

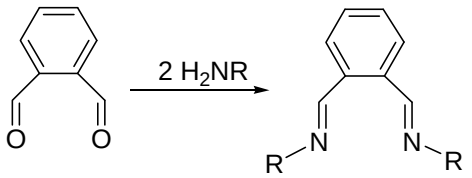
1.6.3 γ-Diimine ligands and their Applications

Neutral γ-diimine ligands analogous to α- and β-diimines are very scarce. Apart from our work, there are currently two reports in the literature that claim to have synthesized γ-diimine ligands. One report, a Japanese patent published by Doi. Y. *et al.* in 1997, claimed to have prepared (γ-diimine)Co(II) complex **110** (Figure 1.27), which polymerized ethylene in the presence of methylaluminoxane.[125] In 2008, another report by Abu-Surrah *et al.* claimed the syntheses and characterization of three γ-diimine ligands (**I**-**K**) and further coordination to form Co(III), Fe(III) and Cr(III) complexes (Scheme 1.31).[126] Abu-Surrah *et al.* also reported preliminary results towards the oxidation of L-cyteine to cystine.



110

Figure 1.27. Proposed Co(II) complexes of γ-diimine by Doi *et al*.[125]



H: R = Ph

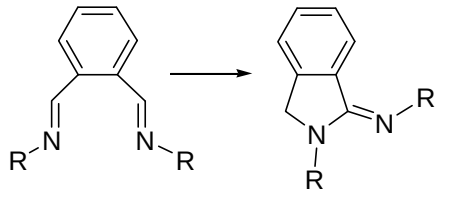
I: R = Cy

J: R = 2-^{i}Pr-C_6H_4

K: R = naphthalyl

Scheme 1.31. Proposed synthesis of γ-diimine ligands by Doi *et al.* and Adnan *et al.* [125, 126]

Given that no NMR or X-ray crystallography data were presented to characterize the ligands or the resultant complexes, it is unlikely that γ-diimine ligands were actually synthesized. Instead, the corresponding iminoisoindolines were likely formed due to intramolecular cyclization (Scheme 1.32). This has been previously reported in the literature and is a general route to the synthesis of iminoisoindolines.[127] Chapter 2 of this manuscript will further discuss this subject.



Scheme 1.32. Intramolecular cyclization of γ-diimines to form iminoisoindolines

1.7 Iminoisoindolines and related compounds

Iminoisoindolines and isoindolinones (Figure 1.28) are products of the condensation reaction of *o*-phthalaldehyde and primary amines and have been known since the early 1900s. In 1910, an iminoisoindoline with R = Ph was the first published example and was reported by Thiele *et al.*[128] Consequently, a large number of its derivatives have been reported since. Moreover, compounds with a phthalimidine (2,3-dihydroisoindol-1-one) skeleton have found applications in medicinal chemistry as anti-inflammatory agents (indoprofen) and antibiotics (staurosporine).[129, 130] N,N'-diaryliminoisoindolines have thus only been used as ligands in transition metal chemistry by our research group. Further details will be discussed in chapter 3.

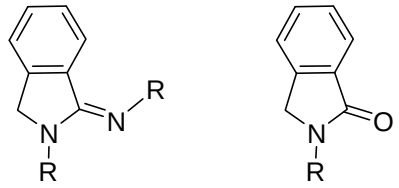


Figure 1.28. General structures of iminoisoindoline and isoindolinone compounds

1.8 Application of α- and β-diimines as ligands in the Formation of Aluminum Alkyl Complexes

Aluminum complexes have been used as active co- and pre-catalysts in polymerization reactions. In organic synthesis, aluminum alkyl compounds are useful as alkylating reagents. Moreover, aluminum alkoxides are among the best catalysts for the ring opening polymerization of cyclic esters. This is an important process because the resultant polymers are biodegradable and have promising practical applications as surgical sutures and environmentally friendly plastics.[131,132] Nitrogen-based bidentate chelating ligands have been explored for many

applications due to their ease of synthesis and electronic/steric tunability of the ligands. In polymerization reactions, these allow control over the molecular weight and microstructure of the resultant polymer.[103-105,133] Consequently, chelating nitrogen-based ligands such as neutral α-diimine (**L**),[134-137] monoanionic β-diketiminate (β-aminoimine) (**M**)[115, 138-146] and dianionic diamido (**N**),[147] amidinate (**O**),[148-150] guanidinate (**P**) and aminotroponiminate (**Q**)[151] ligands (Figure 1.29) have been used in the formation of aluminum alkyl complexes. The advantage with these ligands is the ease with which steric and electronic factors can be modified around the metal centre and are achieved through varying substituents on the nitrogen atoms of the ligand.

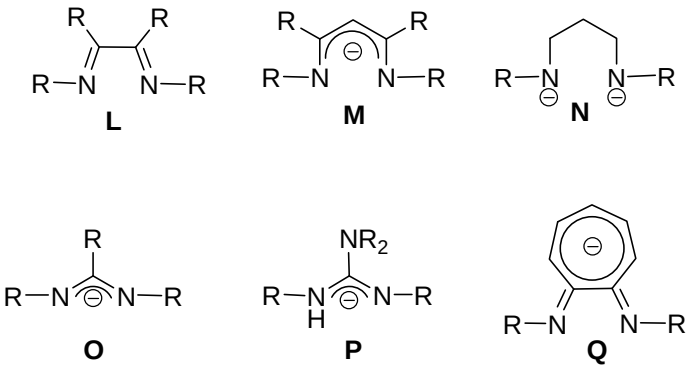
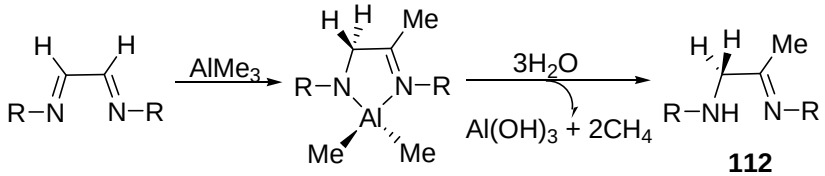


Figure 1.29. Examples of N-based ligands that have been used for formation of aluminum alkyl complexes

1.8.1 α-Diimine-based Aluminum Alkyl Complexes

In 1979, Klerks *et al.* reported the reaction of a series of neutral α-diimine ligands, RN=C(H)-C(H)=NR, [R = $(CH_3)_3C$, 2,4,6-$(CH_3)_3C_6H_2$, 2,6-$(CH_3)_2C_6H_3$] with trimethylaluminum (TMA) to afford coordination products that contained a mono-anionic α-amidoimine ligand in excellent yields (>90%) (Scheme 1.33). Reaction with $AlMe_3$ resulted in an alkylation of the C=N double bond, followed by intramolecular hydrogen transfer to the other imine double bond,

resulting in an amidoimine ligand where the methyl group resides exclusively on the imino functionality and not on the amide (**111a-111c**).[137] They further proposed a way of removing the aluminum by simply carrying out a controlled hydrolysis which results in formation of α-aminoimine ligand **112**. Reports exist in which this technique was applied to obtain ligands that were subsequently coordinated to early transition metals.[152-154]



112

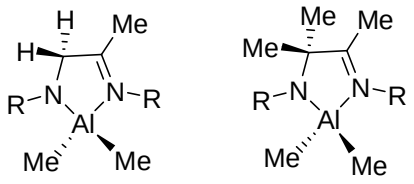
111a: R = Me_3C

111b: R = 2,6-Me_2-C_6H_3

111c: R = 2,4,6-Me_3-C_6H_2

Scheme 1.33. Reaction of α-diimine ligand with trimethylaluminum[137]

Similar results have been reported on other ligands with variations in R-groups and in the ligand backbone.[135, 155-157] Gibson *et al.* and Olson *et al.* reported an extension of Klerks methodology by reacting more sterically hindered α-diimines, RN=C(H)-C(H)=NR and RN=C(Me)-C(Me)=NR (R = 2,6-$^{i}Pr_2C_6H_3$), respectively, to get complexes **113** and **114** (Figure. 1.30).[135, 155] The above work, especially the one reported by Olson *et al.,* motivated us to investigate reactions of aluminum alkyl species with a γ-diimine ligand, which will be discussed in detail in chapters 5 and 6 of this manuscript.



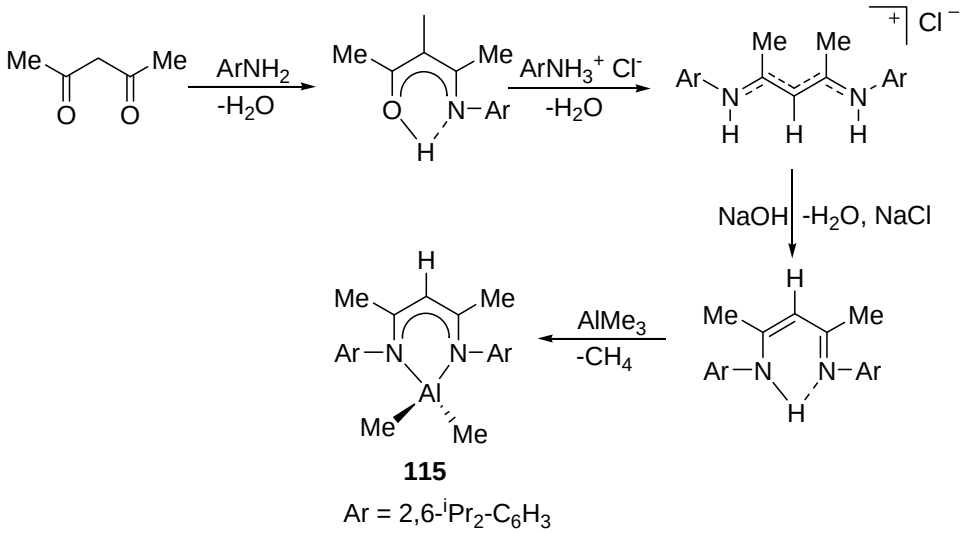
113 **114**

R = 2,6-^{i}Pr$_2$-C$_6$H$_3$

Figure 1.30. α-Amidoimino aluminum alkyl complexes[135, 155]

1.8.2 β-Diimine-based Aluminum Alkyl Complexes

As mentioned earlier, β-diimine ligand **C** (Section 1.6.2, Scheme 1.27), which contains a CH_2 group in its backbone, readily tautomerizes to the enamine isomer. When reacted with aluminum alkyls, it results in deprotonation of the ligand, producing the corresponding β-diketiminato aluminum alkyl complex.[115, 138-146] In 1998 Qian *et al.*[146] reported the synthesis of sterically demanding ligands [HC(C(Me)NAr)$_2$]AlMe$_2$, (Ar = 2,6-^{i}Pr$_2$-C$_6$H$_3$) (**115**) as shown in Scheme 1.34.

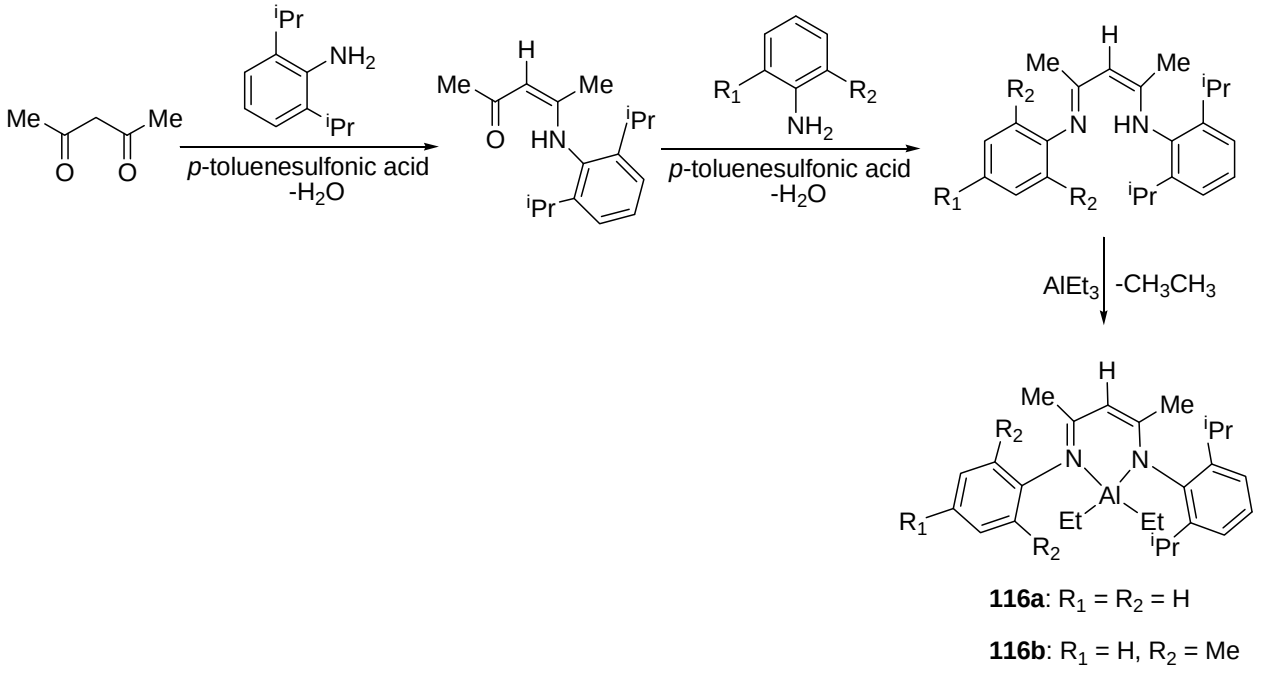


115

Ar = 2,6-^{i}Pr$_2$-C$_6$H$_3$

Scheme 1.34. Synthesis of β-diketiminate ligands and their corresponding aluminum alkyl complexes[146]

Unsymmetrical β-diimine ligands also exist in the literature. Gong *et al.* used a three step synthesis and reported a series of unsymmetrical β-diketiminate and their corresponding aluminum alkyl complexes (**116a**-**116b**, Scheme 1.35).[140] Ligands with differing electron donating abilities on the N-aryl moieties were prepared in a two-step synthesis: one imine nitrogen contains a 2,6-$^{i}Pr_2C_6H_3$ group while there are different substituents on the 2 and 6 positions on the phenyl group attached to the other imine nitrogen. This successful synthesis of unsymmetrical ligands was limited to the reactions of 4-(2,6-diisopropylphenyl)amino-3-penten-2-one with the corresponding aromatic amines. They observed that using other *ortho*-substituents smaller than isopropyl groups (in step one) gave a mixture of compounds which could not be separated.

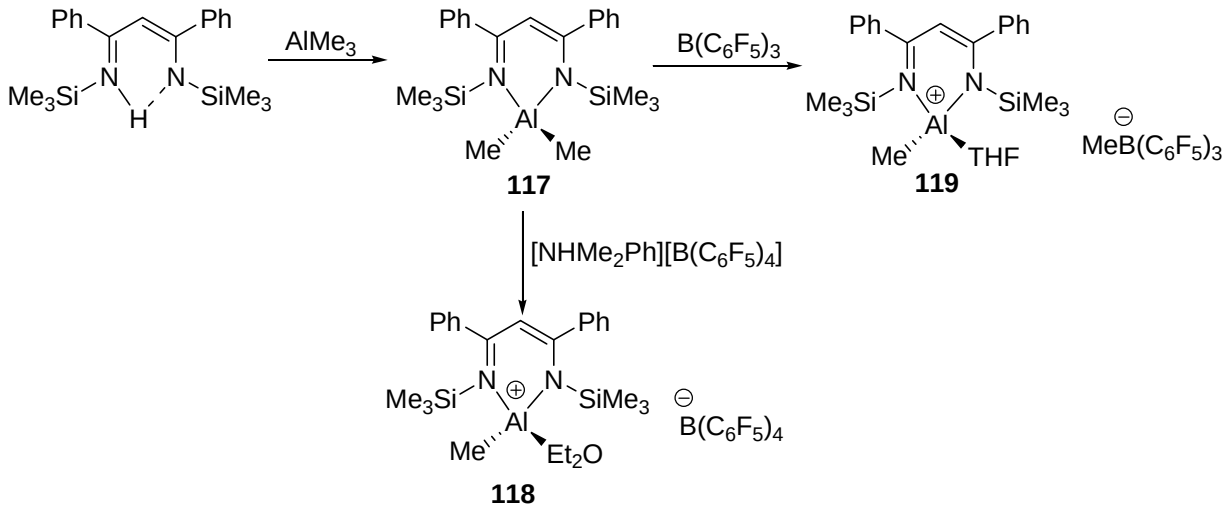


116a: $R_1 = R_2 = H$

116b: $R_1 = H$, $R_2 = Me$

Scheme 1.35. Synthesis of unsymmetrical diimine ligands and their corresponding aluminum alkyl complexes[140]

Cationic aluminum complexes are expected to be highly electrophilic and therefore are of interest for Lewis acid catalysis, olefin polymerization and lactide polymerization. In 1995 Hitchcock *et al.* reported the first X-ray characterized, mononuclear, four-coordinate, cationic alumimum methyl complexes (**118-119)** bearing a β-diketiminate ligand (Scheme 1.36).[145] The ligand, $[H_2C(C(Ph)NR)_2]AlMe_2$, (R = $SiMe_3$) was modified in the backbone by placing phenyl groups on the imine carbon and trimethylsilyl groups on the imine nitrogen. Reaction of the ligand with $AlMe_3$ gave the corresponding aluminum alkyl complexes. The mononuclear four-coordinate cationic methylaluminum complex **118** was obtained by treating dimethylaluminum complex **117** with tris(pentafluorophenyl)borane. A similar cationic methylaluminum complex (**119**) was obtained when *N,N*-dimethylanilinium tris(pentafluorophenyl)borate was used as the dealkylating agent.

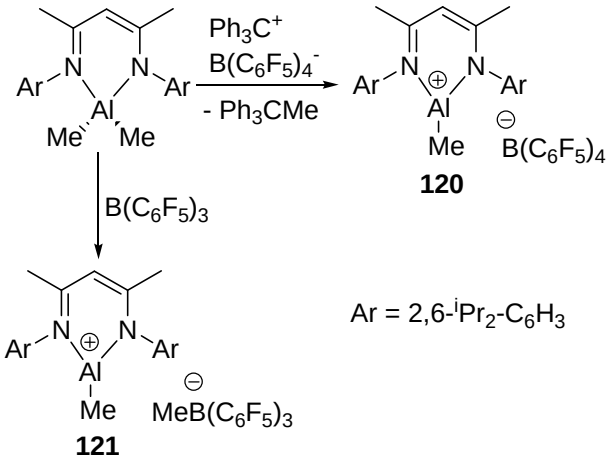


Scheme 1.36. Formation of cationic aluminum species using β-diketimine ligand[145]

Utilizing different methyl abstraction agents, a number of cationic methyl aluminum complexes have also been reported. Radzewich *et al.* reacted $\{HC(C(Me)NAr)_2\}AlMe_2$, (Ar =

2,6-$^{i}Pr_2$-C_6H_3) with $[Ph_3C][B(C_6F_5)_4]$ to produce $[\{HC(C(Me)NAr)_2\}AlMe][B(C_6F_5)_4]$ (**120**) through methyl abstraction (Scheme 1.37). In addition, a compound $[\{HC(C(Me)NAr)_2\}AlMe][MeB(C_6F_5)_4]$ (**121**) with a different counterion was obtained when the aluminum complex was reacted with $B(C_6F_5)_3$.[144]

There are no reports in the literature on reaction of γ-diimine ligands with aluminum species to form γ-amidoimino or γ-diimino aluminum alkyl complexes. This topic will be the focus of chapters 5 and 6 of this thesis.



Scheme 1.37. Synthesis of cationic aluminum alkyl species[144]

1.9 Research Objectives

As mentioned earlier, group 10 metal complexes of α- and β-diimine ligands have been extensively studied as precatalysts for olefin polymerization and C-C coupling reactions. On the other hand, complexes with γ-diimine ligands analogous to α- and β-diimine did not exist when we started this project. It is worth reiterating that the only report (a Japanese patent) that claimed to have synthesized a (γ-diimine)Co(II) complex as an active precatalyst for olefin polymerization did not present any spectral evidence for the ligand and the corresponding complex. Moreover, β-

diimine ligands were found to be inferior towards stabilization of palladium precursors compared with α-diimine ligands. This was attributed to the absence of conjugation in β-diimine complexes. Therefore, the primary objective of this project was to synthesize and fully characterize a series of γ-diimine ligands and investigate their reactivity with group 10 metals. The expected seven-membered complexes would then be tested in olefin polymerization reactions and their reactivity would be compared to their α- and β-diimine counterparts. This is the focus of Chapter 2.

The second research objective arose directly from the first one. We managed to synthesize and fully characterize only one γ-diimine ligand from the reaction of phthalaldehyde with a bulky aniline, 2,6-$^{i}Pr_2C_6H_3NH_2$. Any aniline with less bulky substituents on the *ortho*-position resulted in formation of iminoisoindoline ligands, which are the cyclized form of γ-diimine ligands (Scheme 1.32). Moreover, when the γ-diimine ligand was reacted with $Pd(OAc)_2$, a five-membered dinuclear palladacyclic complex formed instead of seven-membered (γ-diimine)Pd(II) complex. This was found to be an active precatalyst for C-C coupling reactions. The second objective was therefore to synthesize and fully characterize six-membered dinuclear *Ar,Ar'*-diaryl-2-iminoisoindoline-based (Ar = Ar', Figure 1.31) palladacyclic complexes for C-C coupling reactions. Motivation for this objective came from the fact that palladacycles are among the most active precatalysts for C-C coupling reaction in the literature. These results are described in Chapter 3.

As was shown in Section 1.4 of this introduction, there is evidence that shows that mononuclear palladacyclic species are more active than their corresponding dinuclear palladacyclic species towards C-C coupling reactions. The third research objective therefore, was to synthesize phosphine-ligated mononuclear *Ar,Ar'*-diaryl-2-iminoisoindoline-based palladacycles (Ar = Ar') and compare their catalytic activities towards C-C coupling reactions with their corresponding dinuclear complexes as described in Chapter 4.

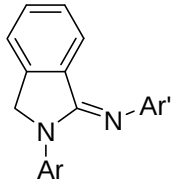


Figure 1.31. Iminoisoindoline ligands

We concluded from the second research objective that the iminoisoindoline ligand obtained from the reaction of phthalaldehyde with *p*-nitroaniline was unreactive towards Pd(II) precursors. This was attributed to reduced electron density on the imine nitrogen due to the highly electron withdrawing ability of the nitro group on the *para*-position on the benzene ring. The fourth research objective was then to synthesize a series of "mixed" *Ar,Ar'*-diaryl-2-iminoisoindolines [Ar ≠ Ar' = *p*-NO_2-C_6H_3] (Figure 1.31), where the aryl group on the imine nitrogen would contain a nitro group while the other aryl moiety on the nitrogen in the iminoisoindoline ring would contain an aryl group with a more electron donating substituent, employing a one-step, three-component reaction. The research question here was this: could mixed diaryliminoisoindolines be synthesized, and if so, could palladacycles be synthesized if only one aryl group contained a *p*-nitro functionality and how would this affect C-C coupling activity? These questions are addressed in Chapter 5.

The reaction of α-diimine ligands with trimethylaluminum ($AlMe_3$) results in formation of (α-aminoimino)$AlMe_2$ complexes through aluminum coordination and methylation of the imine carbon by a methyl group from trimethylaluminum. The fifth research objective was to determine factors and conditions by which γ-amidoimino and γ-diimine complexes of alkyl/halide aluminum could be synthesized and to explore the reactivity of these complexes in the polymerization of lactones. Chapters 6 and 7 will focus on these topics.

1.10 Organization and Scope

This Ph.D. thesis is primarily concerned with ligands derived from attempts to synthesize a series of γ-diimine ligands and subsequent applications of these ligands in palladium and aluminum coordination chemistry and catalysis. It is divided into 8 chapters. Chapters 2-4 are verbatim copies of articles published in the literature, while chapters 5-7 are manuscripts ready for submission. Before each chapter, there is an introductory section that describes what that particular chapter is about, the author's contributions, and a paragraph connecting that chapter to the overall objectives of this Ph.D. thesis.

Chapter 1 presented an overview of mononuclear and dinuclear palladacycles with different donor atoms (P, S, N, O and Se) and their applications in C-C coupling reactions. Additionally, it discussed diimine ligands and their contribution to ethylene polymerization and as precatalysts in C-C coupling reactions.

Chapter 2 presents the synthesis of the first structurally characterized γ-diimine ligand and applications of the ligand in formation of group 10 coordination complexes and subsequent palladacycle formation along with C-C coupling studies. It was during the course of these studies that iminoisoindoline formation was observed from intramolecular cyclization of γ-diimines.

Chapter 3 presents the synthesis of *Ar,Ar′*-diaryliminoisoindolines (Ar = Ar', Figure 1.31) and their application in the preparation of *ortho*-metallated dinuclear palladium complexes. This class of ligand has not previously been investigated in any kind of coordination chemistry.

Chapter 4 presents phosphine-ligated mononuclear iminoisoindoline-based palladacycles of the general formula [Pd(iminoisoindoline)X(PR_3)], X= OAc or Cl, R = Ph or Cy.

Chapter 5 presents the syntheses and characterization of mixed *Ar,Ar′*-mixed-diaryliminoisoindolines, wherein the two aryl groups of the iminoisoindoline ligands contain

different substituents (Ar ≠ Ar', Figure 1.31) obtained from a one-step, three-component reaction. Results from the catalytic studies towards the C-C coupling reaction are also presented.

Chapter 6 presents the step-by-step syntheses of aluminum alkyl complexes obtained from the reaction of trimethylaluminum, TMA, with γ-diimine ligands.

Chapter 7 presents the continuation of the syntheses of neutral and cationic aluminum alkyl complexes obtained from the reaction of aluminum species ($AlMe_2Cl$, $AlMeCl_2$ and $AlCl_3$) with a γ-diimine ligand.

Chapter 8 presents a summary, conclusion and future work.

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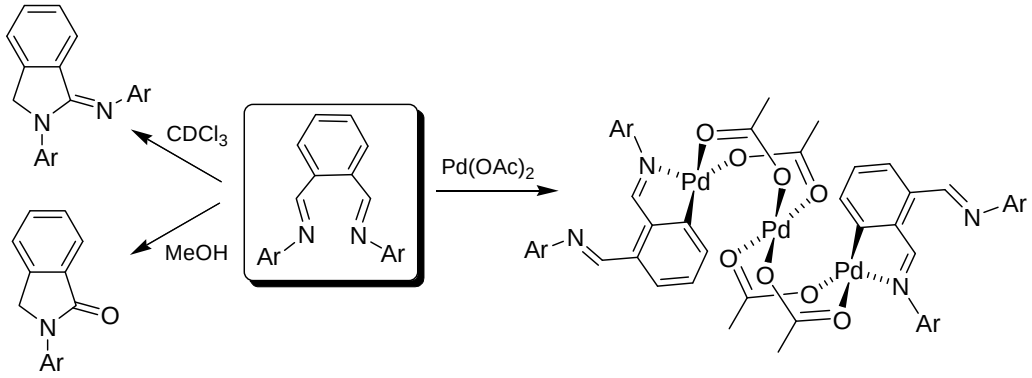
CHAPTER 2

PUBLICATION 1

Description

The following is a verbatim copy of an article that was published in April of 2008 in an American Chemical Society Journal (*Organometallics*, **2008**, *27*, 2337-2345) and describes the synthesis and characterization of a novel γ-diimine ligand and its corresponding palladium chloride and acetate complexes. The application of the two complexes in catalysis of the Suzuki and Heck coupling reactions is also described.



Authors' Contribution

I synthesized all the organic compounds and transition metal complexes, and also conducted Suzuki and Heck C-C coupling reactions using [(γ-diimine)PdCl(μ-Cl)]$_2$ (**5**). Demyan E. Prokopchuk, for his summer project, conducted some of the catalytic studies employing the {1,2-(2,6-^{i}Pr$_2$-C$_6$H$_3$N=CH)$_2$-C$_6$H$_3$]Pd(μ-OAc)$_2$}$_2$Pd (**6**). Dr. J. Wilson Quail did all the structure determination by single crystal X-ray analysis and the work was supervised by Dr. Stephen R. Foley. Written permission was obtained from all contributing authors and the publisher to include this material within this thesis.

Relation of Chapter 2 (Publication 1) to the overall Objectives of this Project

As mentioned in the introduction, the first research objective was to synthesize and fully characterize a series of γ-diimine ligands and investigate their reactivity towards group 10 transition metals. However, only one γ-diimine ligand, $(2,6\text{-}^{i}Pr_2C_6H_3N{=}CH)_2C_6H_4$ (**2**), was isolated from the reaction of *o*-phthaladehyde and a bulky aniline, 2,6-diisopropylaniline. It is also observed that any aniline with less bulky substituents on the *ortho* position of the aniline resulted in formation of iminisoindoline ligands. In addition, reaction of the γ-diimine ligand with $PdCl_2$ did not result in a seven-membered coordination complex, but in non-palladacyclic complex, $[(\gamma\text{-diimine})PdCl(\mu\text{-}Cl)]_2$ (**5**). Reaction with $Pd(OAc)_2$ gave an S-shaped five-membered trinuclear palladacyclic complex, $\{1,2\text{-}(2,6\text{-}^{i}Pr_2\text{-}C_6H_3N{=}CH)_2\text{-}C_6H_3]Pd(\mu\text{-}OAc)_2\}_2Pd$ (**6**).

2. From Pyrroles to Isoindolines: Synthesis of a γ-diimine Ligand for Applications in Palladium Coordination Chemistry and Catalysis

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2.1 Abstract

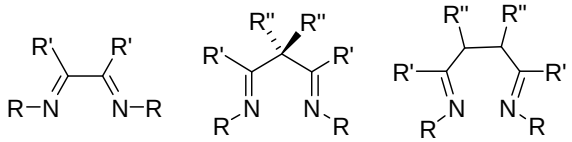
The γ-diimine, 1,2-(2,6-$^{i}Pr_2$-$C_6H_3NCH)_2$-C_6H_4 (**2**), was synthesized by the reaction of phthalaldehyde with 2,6-diisopropylaniline. Depending on reaction conditions **2** can cyclize to form the corresponding iminoisoindoline or isoindolinone. Unlike analogous α- and β-diimine complexes, reaction of the γ-diimine **2** with $(MeCN)_2PdCl_2$ results in a dinuclear complex, [(γ-diimine)PdCl(μ-Cl)]$_2$ (**5**), where the ligand does not coordinate to the Pd(II) center in a chelating fashion but instead adopts a monodentate coordination mode. On the other hand, reaction of **2** with $Pd(OAc)_2$ results in C-H activation and formation of a trinuclear $Pd_3(OAc)_4$-based palladacycle {1,2-(2,6-$^{i}Pr_2$-$C_6H_3NCH)_2$-C_6H_3]Pd(μ-OAc)$_2$}$_2$Pd (**6**). The resulting palladium complexes were tested as precatalysts in Heck and Suzuki coupling reactions.

2.2 Introduction

α-Diimines based on 1,4-diazabutadienes of the general formula RN=CR'-CR'=NR have received considerable attention in recent years due to their application as ligands in a wide variety of catalytic reactions. It was initial reports by Brookhart in the field of olefin polymerization and olefin/CO copolymerization using Ni(II) and Pd(II) complexes that have initiated the widespread interest in applications of these diimines as ligands.[1-14] Group 10 complexes with diazabutadiene ligands showed higher activities than the classical Ziegler catalysts and exhibited a greatly reduced susceptibility to poisoning by polar functionalities.[15] Pd(II) complexes of diimines have also been reported to be active catalysts for the Suzuki, Heck, Sonogashira and Hiyama coupling reactions.[9, 16-18]

This class of ligand has become increasingly popular due to its ease of synthesis and outstanding steric and electronic tunability. The most common synthetic route to diimine ligands is a simple condensation reaction of primary amines or anilines with diketones or dialdehydes, thereby producing a wide range of α- and β-diimines (Figure 2.1).

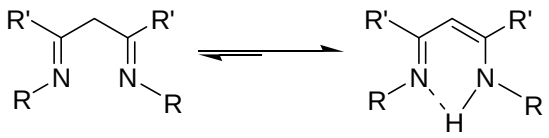
Figure 2.1.



In 1997, β-diimine ligands analogous to Brookhart's α-diimines were synthesized and their reactivity explored in the formation of group 10 complexes.[19] β-Diimines are usually best

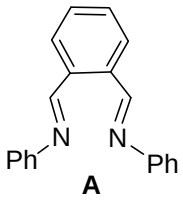
interpreted as β-diketimines due to the acidic nature of the methylene protons (Scheme 2.1) and have been successfully employed as monoanionic ligands in a wide variety of reactions.[20-27]

Scheme 2.1



β-Diimine variations in which the acidic protons have been substituted by alkyl groups to form stable neutral ligands have recently been reported.[21,22,25] The corresponding Pd(II) complexes were found to be active precatalysts for C-C coupling reactions.[22]

There is one report in the patent literature concerning the synthesis of a cobalt complex of **A** which polymerizes ethylene in the presence of methylaluminoxane.[15, 28]



A

This represents the only report of a γ-diimine in the published literature. Analogous γ-diimines have, however, been proposed as intermediates in the synthesis of iminoisoindolines and isoindolinones.[29-34] We initially envisioned that the synthesis of γ-diimine compounds might be a general reaction leading to a new class of diimine ligands, however intramolecular cyclization reactions have to date inhibited this notion. Herein we report the synthesis of a γ-diimine ligand and subsequent formation of Pd(II) complexes. Depending on reaction conditions, cyclization of

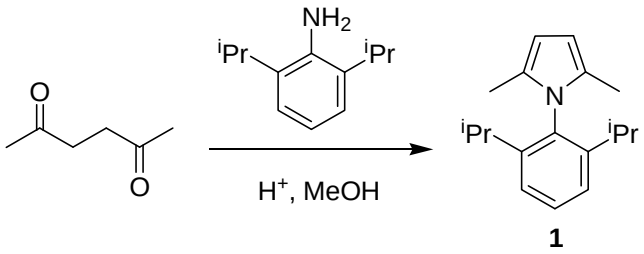
the γ-diimine can be induced to form either the corresponding iminoisoindoline or the isoindolinone. The resulting (γ-diimine)Pd(II) complexes were tested as precatalysts for Suzuki and Heck coupling reactions.

2.3 Results and Discussion

2.3.1 Synthesis of a γ-diimine

Attempts to synthesize a γ-diimine ligand from a simple diketone such as 2,5-hexanedione and 2,6-diisopropylaniline in acidified methanol yielded only the pyrrole (**1**) via a Paal-Knorr synthesis as the sole product regardless of stoichiometry (Scheme 2.2). The same pyrrole was recently synthesized employing metal triflates as catalysts.[35]

Scheme 2.2



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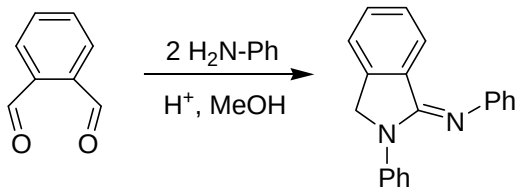
Use of a constrained dialdehyde such as phthalaldehyde should inhibit pyrrole formation possibly allowing for isolation of the desired γ-diimine. As mentioned earlier, reactions of phthalaldehyde with primary amines have been known for several decades and usually result in formation of the corresponding iminoisoindoline or isoindolinone depending on reaction conditions. While γ-diimines have been postulated as intermediates in the formation of iminoisoindolines or isoindolinones, only γ-diimine **A** has ever been isolated.[28-34]

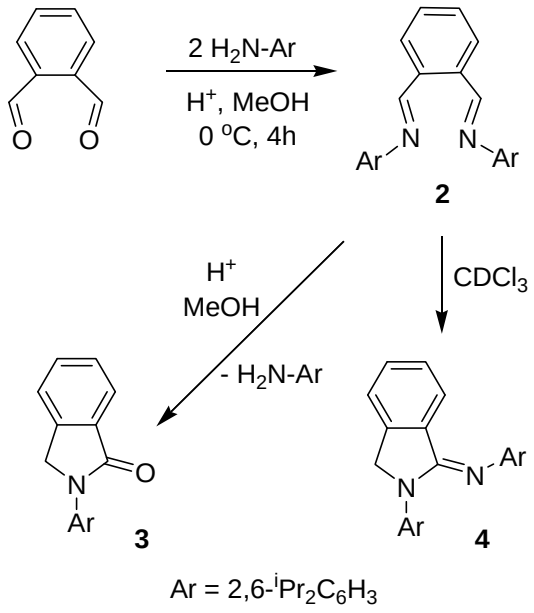
In our hands, all attempts to synthesize γ-diimine **A** were unsuccessful yielding only the previously reported iminoisoindoline, 1-phenylimino-2-phenylisoindoline, according to Scheme 2.3.[29]

Scheme 2.3



It appears unlikely that γ-diimine **A** was ever actually isolated as it would be prone to rapid intramolecular cyclization to the corresponding iminoisoindoline. Increasing the steric bulk on the nitrogen positions via condensation with a bulky primary amine should however retard or inhibit intramolecular cyclization allowing for isolation of a γ-diimine. Thus, a γ-diimine was prepared through the reaction of phthalaldehyde with 2,6-diisopropylaniline in methanol to yield the corresponding phthalaldimine, 1,2-(2,6-$^{i}Pr_2$-$C_6H_3N{=}CH)_2$-C_6H_4 (**2**), as a yellow precipitate in 66% yield (Scheme 2.4). The remaining products in the filtrate consisted only of the isoindolinone **3** (30 % yield) and 2,6-diisopropylaniline. ^{1}H NMR of **2** in $CDCl_3$ showed one singlet downfield at δ 8.78 integrating for two protons for the imine, *H*C=N while ^{13}C NMR showed one signal at δ 161.8 for the imine indicative of a C_{2v} symmetric species in solution at room temperature. FT-IR spectroscopy showed a single C=N stretch at 1633 cm^{-1}.

Scheme 2.4



The solid state structure of **2** has been determined by X-ray diffraction and is depicted in Figure 2.2. Selected interatomic distances are provided in Table 2.1. Unlike the proposed solution structure, the solid state structure of **2** has C_s symmetry and crystallizes preferentially as rotamer **b** (Scheme 2.5) where one imine is rotated into a cisoidal orientation whereas the other imine adopts a transoidal orientation. The solution data indicates however that the barrier to rotation between the three possible rotational conformers depicted in Scheme 2.5 is low at room temperature resulting in fast interconversion between the rotamers and an average structure with C_{2v} symmetry. While variable-temperature ^{1}H NMR spectra support the fluxional behavior of **2** as seen in Figure 2.3, even at 183 K the static limit for rotational isomerization had not been reached and discrete rotational isomers were not observed. At 296 K one doublet at δ 1.08 for the methyl groups is observed along with a sharp singlet at δ 8.78 for the imine protons. The ^{1}H NMR

spectra at 183 K showed the methyl groups as two discrete broad resonances while the signal for the imine protons exhibited line broadening.

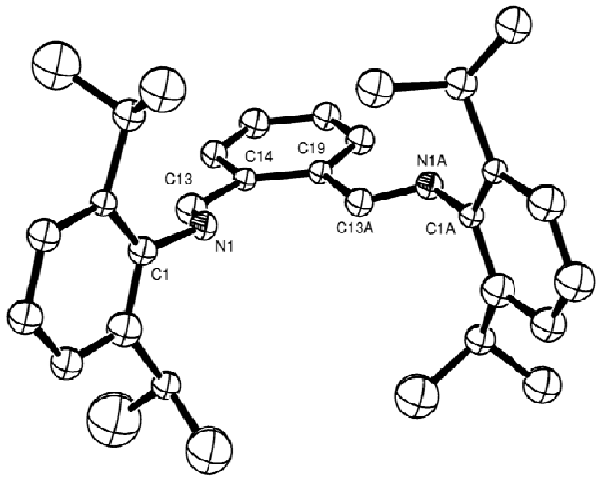
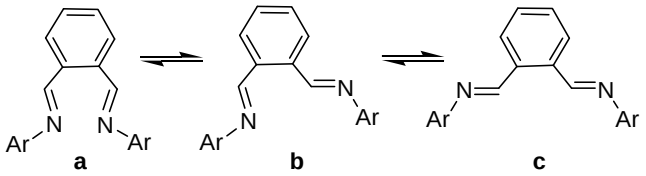


Figure 2.2. ORTEP plot of γ-diimine (**2**) at the 50% probability level. The hydrogen atoms have been omitted for clarity.

Table 2.1. Selected bond distances (Å) and angles (º) for γ-diimine (**2**)

Bond distances (Å)		**Bond angles (º)**	
N(1)-C(13)	1.250(15)	C(13)-N(1)-C(1)	118.6(9)
N(1)-C(1)	1.395(10)	C(13A)-N(1A)-C(1A)	120.1(9)
N(1A)-C(13A)	1.280(13)	N(1)-C(13)-C(14)	125.8(9)
N(1A)-C(1A)	1.424(11)	N(1A)-C(13A)-C(19)	120.4(9)

Scheme 2.5



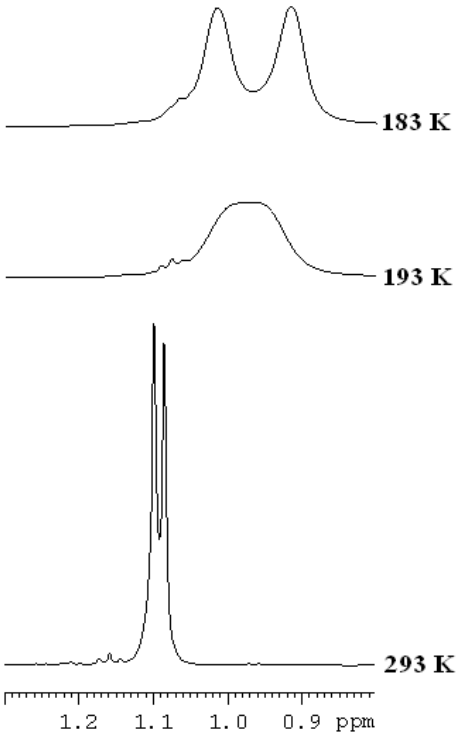


Figure 2.3. Variable-temperature ^{1}H NMR (CD_2Cl_2) study of γ-diimine **2** focusing on the methyl signals of the isopropyl groups (residual ether is observed immediately downfield of methyl resonances).

Interestingly, if **2** is not isolated as a precipitate from the methanolic solution, it further reacts by redissolving back into solution to form the corresponding isoindolinone **3**, and one equiv of 2,6-diisopropylaniline. Thus, the yield of **2** decreases favoring formation of isoindolinone **3** at

longer reaction times. Isoindolinone **3** can be directly synthesized by reaction of phthalaldehyde with one equiv 2,6-diisopropylaniline at ambient temperature in 75% yield. γ-Diimine **2** is however stable in non-polar organic solvents in the absence of protic acids for prolonged periods. ^{1}H NMR of the isoindolinone **3** in $CDCl_3$ showed a characteristic singlet at δ 4.56 for the two methylene protons. The solid state structure of **3** has been determined by X-ray diffraction and is depicted in Figure 2.4. Selected interatomic distances are provided in Table 2.2. The structure of **2** has been previously communicated.[36]

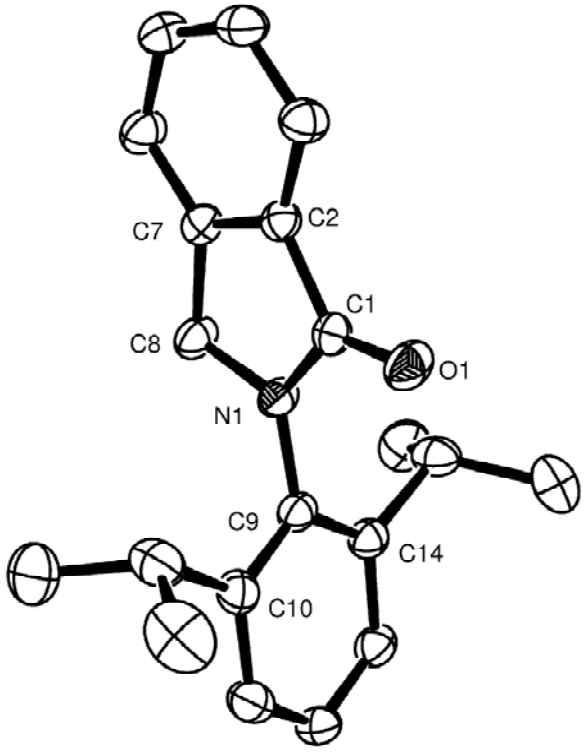


Figure 2.4. ORTEP plot of isoindolinone (**3**) at the 50% probability level. The hydrogen atoms have been omitted for clarity.

Table 2.2. Selected bond distances (Å) and angles (º) for isoindolinone (**3**).

Bond distances (Å)	**Bond angles (º)**
O(1)-C(1) 1.223(2)	C(1)-N(1)-C(9) 125.86(12)
N(1)-C(1) 1.362(2)	C(1)-N(1)-C(8) 113.52(12)
N(1)-C(9) 1.362(19)	C(9)-N(1)-C(8) 120.62(12)
N(1)-C(8) 1.362(19)	O(1)-C(1)-N(1) 125.96(14)
	O(1)-C(1)-C(2) 128.13(15)

Slow cyclization of γ-diimine **2** to form the corresponding iminoisoindoline **4** in quantitative yield is observed in $CDCl_3$ (Scheme 2.4). Presumably the reaction is catalyzed by trace DCl present in the solvent. Observation of **2** by ^1H NMR spectroscopy in $CDCl_3$ showed that over the course of 12 h at 60 °C, 50 % of the γ-diimine underwent cyclization to form the corresponding iminoisoindoline (**4**). Heating for an additional 12 h resulted in quantitative cyclization of **2** to the iminoisoindoline (Figure 2.5). ^1H NMR spectra of **4** in $CDCl_3$ showed a characteristic singlet at δ 4.69 for the two methylene protons.

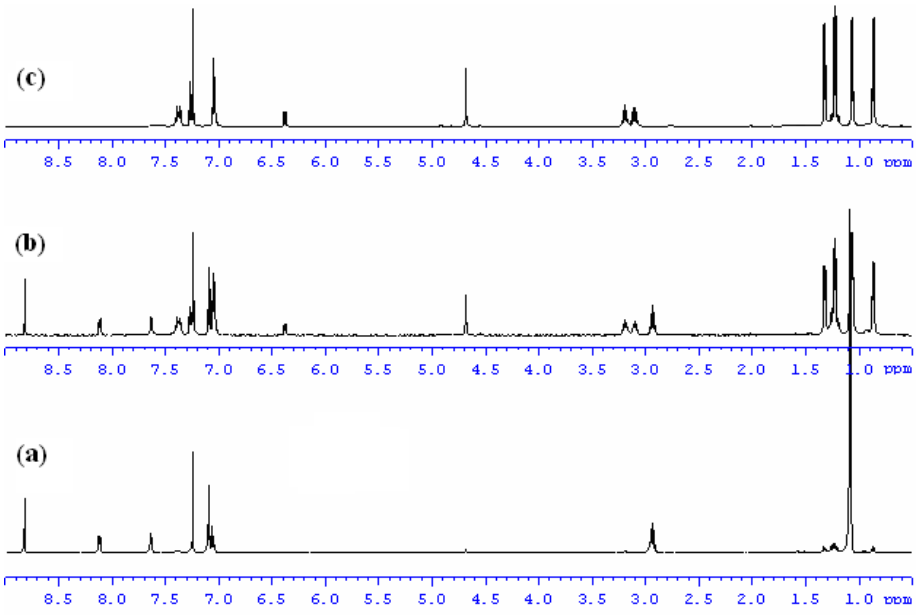


Figure 2.5. ^{1}H NMR ($CDCl_3$) spectra showing the cyclization of γ-diimine **2** to iminoisoindoline **4** at 60 °C. (a) γ-diimine **2** at t = 0.25 h. (b) 1:1 mixture of **2** and **4** observed at t = 12 h. (c) complete cyclization to **4** observed at t = 24 h.

Prolonged exposure of iminoisoindoline **4** to $CDCl_3$ resulted in precipitation of the DCl salt of iminoisoindoline (**4·DCl**) as X-ray quality crystals. The solid state structure of **4·DCl** was subsequently determined by X-ray diffraction and is depicted in Figure 2.6. Selected interatomic distances are provided in Table 2.3. The iminoisoindoline bicyclic ring is lying on a mirror plane. The two diisopropylphenyl moieties are bisected by the mirror plane and are thus perpendicular to the primary isoindoline ring.

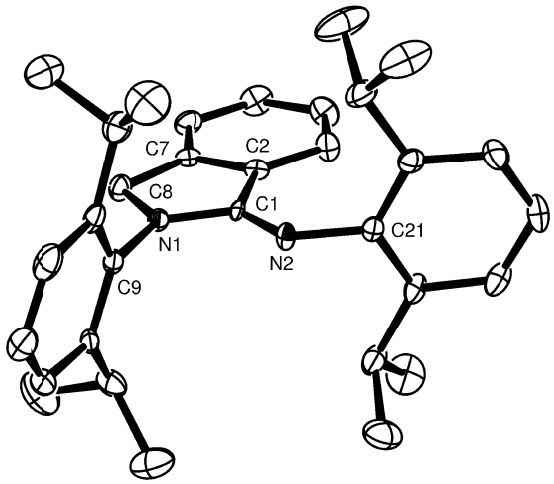


Figure 2.6. ORTEP plot of **4-DCl·CDCl$_3$** at the 50% probability level. The hydrogen/deuterium atoms, chloride counter-ion and solvent molecule have been omitted for clarity.

Table 2.3. Selected bond distances (Å) and angles (º) of **4-DCl·CDCl$_3$**.

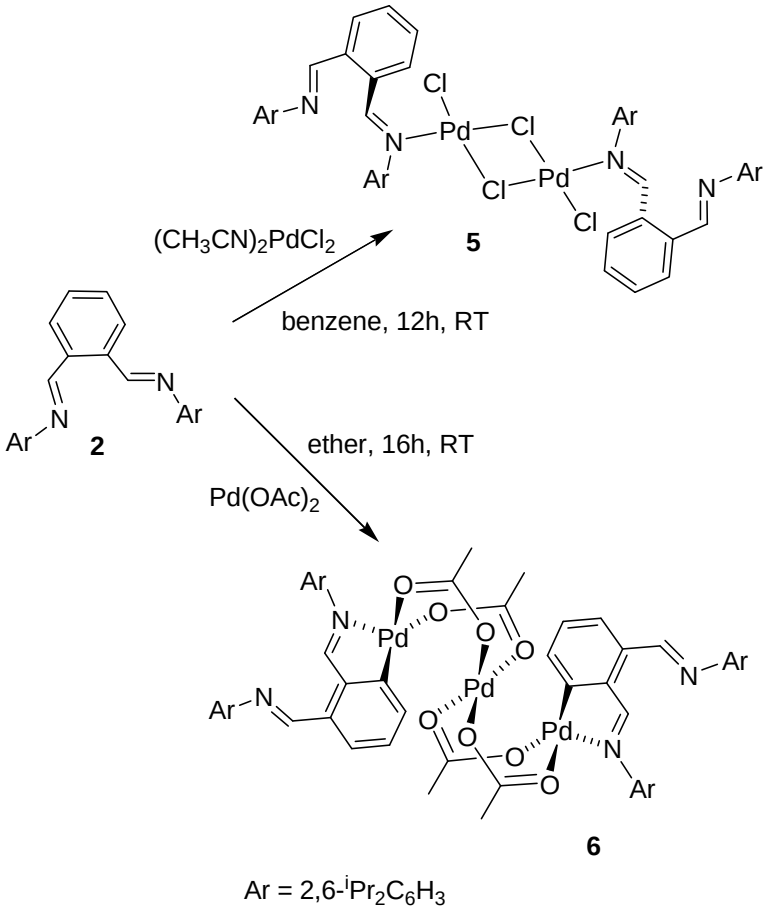
Bond distances (Å)		**Bond angles (º)**	
N(1)-C(1)	1.345(3)	C(1)-N(1)-C(9)	126.1(2)
N(1)-C(9)	1.442(3)	C(1)-N(1)-C(8)	112.9(2)
N(1)-C(8)	1.469(4)	C(9)-N(1)-C(8)	121.0(2)
N(2)-C(2)	1.304(4)	C(1)-N(2)-C(21)	120.6(2)
N(2)-C(16)	1.441(3)	N(2)-C(1)-N(1)	123.3(2)

2.3.2 (γ-diimine)Pd(II) Complexes

Reaction of γ-diimine ligand **2** with $(CH_3CN)_2PdCl_2$ in benzene afforded the dinuclear (γ-diimine)Pd(II) complex, $[(\gamma\text{-diimine})PdCl(\mu\text{-Cl})]_2$ (**5**), as an orange solid in 47% yield (Scheme

2.6). The reaction also proceeded with [(cyclooctene)$PdCl_2$]$_2$ as the $PdCl_2$ source however no reaction was observed if (cyclooctadiene)$PdCl_2$ is employed. Complex **5** was air stable in both non-coordinating solvents and in the solid state. The γ-diimine did not coordinate in a chelating mode but instead acted as a monodentate ligand with one imine remaining uncoordinated as evidenced by ^{1}H, ^{13}C NMR and IR spectroscopic studies. It is worthwhile to note that a reported (diphosphaalkene)Pd(II) analogue showed the diphosphaalkene ligand coordinating in a bidentate fashion forming a 7-membered ring.[37] ^{1}H NMR of **5** in $CDCl_3$ showed two characteristic singlets appearing downfield at δ 8.25 and δ 8.17 indicating that the two imine (*H*C=N) protons were no longer equivalent.

Scheme 2.6



^{13}C NMR spectra showed that the chemical shift for the coordinated imine carbon (H*C*=N) had shifted downfield to δ 176.0 while the uncoordinated imine remained upfield at δ 161.8. Similarly, two C=N stretches were observed by FT-IR spectroscopy. One C=N stretch appeared at 1633 cm^{-1} corresponding to the uncoordinated imine while the other C=N stretch was observed at 1618 cm^{-1} consistent with coordination of an imine nitrogen atom to an electrophillic metal center. The solid state structure of **5** has been determined by X-ray diffraction and is depicted in Figure 2.7. Selected interatomic distances are provided in Table 2.4. The structure revealed that **5** is a dinuclear chloride bridged complex with a slightly distorted square planar coordination geometry about each palladium atom. The environment around each palladium consists of two

bridging chlorides, one terminal chloride and a monodentate γ-diimine ligand with one of the ligand imine functionalities remaining uncoordinated. The ligand again preferentially adopts the same rotational conformer as that of the solid state structure of the free ligand thereby effectively inhibiting a bidentate coordination mode to the metal center.

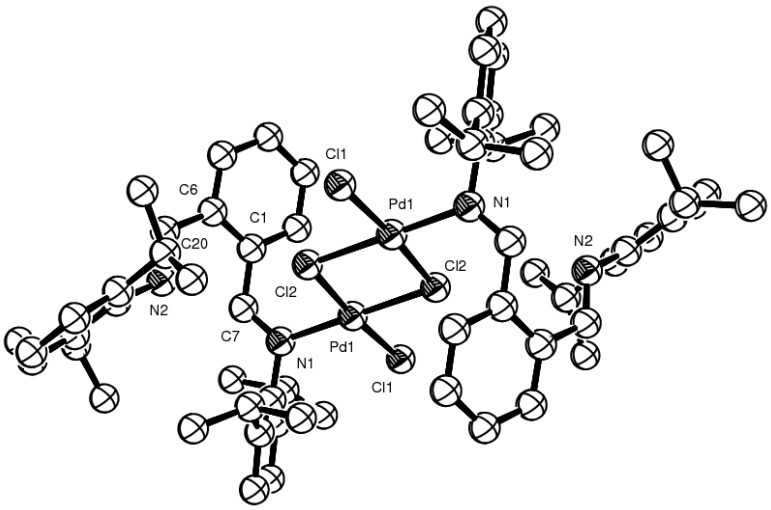


Figure 2.7. ORTEP plot of **5** at the 50% probability level. The hydrogen atoms have been omitted for clarity.

Table 2.4. Selected bond distances (Å) and angles (º) of **5**.

Bond distances (Å)		**Bond angles (º)**	
Cl(1)-Pd(1)	2.2796(9)	Pd(1)-Cl(2)-Pd(1)'	95.37(3)
Cl(2)-Pd(1)	2.3141(9)	C(7)-N(1)-Pd(1)	122.6(2)
Cl(2)-Pd(1)'	2.3338(9)	N(1)-Pd(1)-Cl(1)	90.79(8)
N(1)-C(7)	1.276(4)	N(1)-Pd(1)-Cl(2)	177.26(9)
N(1)-C(8)	1.456(4)	Cl(1)-Pd(1)-Cl(2)	91.15(3)
N(1)-Pd(1)	2.028(3)	N(1)-Pd(1)-Cl(2)'	93.50(8)
N(2)-C(20)	1.259(5)	Cl(1)-Pd(1)-Cl(2)'	175.34(4)
N(2)-C(21)	1.433(5)	Cl(2)-Pd(1)-Cl(2)'	84.63(3)

Reaction of γ-diimine **2** with $Pd(OAc)_2$ in ether at ambient temperature for 16 h affords the air stable five-membered palladacyclic species **6** as an orange solid (Scheme 2.6). Contrary to the reaction with $(MeCN)_2PdCl_2$ or $[(cyclooctene)PdCl_2]_2$, where no C-H activation of the ligand is observed, ortho-cyclopalladation readily occurs when $Pd(OAc)_2$ is employed as the Pd(II) source. ^{1}H NMR of **6** showed two distinct singlets at δ 9.50 and 8.09 for the coordinated and uncoordinated imine protons (*H*C=N) respectively, as well as four bridging acetate ligands. The identity of the complex was further established by X-ray diffraction studies. Most interestingly, the complex possesses a rare $Pd_3(OAc)_4$ core, which results in an S-shaped complex (Figure 2.8 and 2.9). To our knowledge this is the fifth example of structurally characterized $Pd_3(OAc)_4$-containing complex.[38-41] Selected bond distances and angles are shown in Table 2.5. The Pd-C

distance of 1.949(6) Å is consistent with the previously reported $Pd_3(OAc)_4$-based complexes as is the Pd-Pd distance of 2.9721(6) Å.

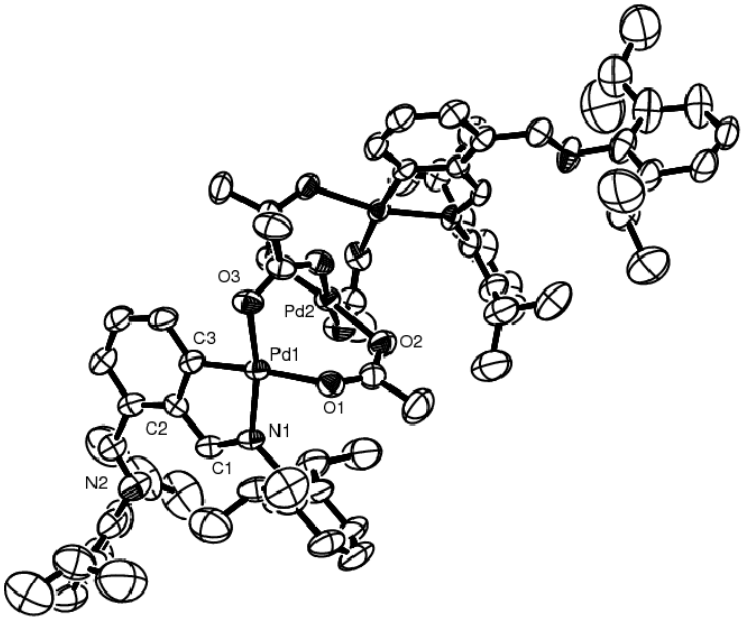


Figure 2.8. ORTEP plot of **6** at the 50% probability level. The hydrogen atoms have been omitted for clarity.

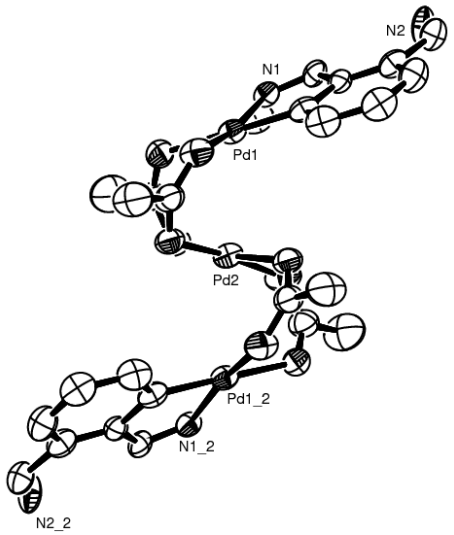


Figure 2.9. ORTEP plot of **6** at the 50% probability level illustrating the S-shape derived from the $Pd_3(OAc)_4$ core. The 2,6-$^{i}Pr_2$-C_6H_3 groups and hydrogen atoms have been omitted for clarity.

Table 2.5. Selected bond distances (Å) and angles (º) of **6**.

Bond distances (Å)		**Bond angles (º)**	
Pd(1)-C(3)	1.949(6)	C(3)-Pd(1)-N(1)	81.1(2)
Pd(1)-N(1)	2.018(4)	C(3)-Pd(1)-O(3)	92.57(19)
Pd(1)-O(3)	2.057(4)	N(1)-Pd(1)-O(3)	166.51(7)
Pd(1)-O(1)	2.127(4)	C(3)-Pd(1)-O(1)	174.59(19)
Pd(1)-Pd(2)	2.9721(6)	N(1)-Pd(1)-O(1)	93.67(17)
Pd(2)-O(2)	2.127(4)	O(3)-Pd(1)-O(1)	92.83(17)
Pd(2)-O(2)’	2.013(4)	C(1)-N(1)-Pd(1)	114.5(3)
Pd(2)-O(4)’	2.019(4)		

Table 2.6. Crystal data and refinement parameters for compounds **2** to **6**.

	2	**3**	**4**-$DCl{\cdot}CDCl_3$	**5**·$2CHCl_3$	**6**·$2CH_2Cl_2$
formula	$C_{32}H_{40}N_2$	$C_{20}H_{23}NO$	$C_{33}H_{40}D_2Cl_4N_2$	$C_{66}H_{82}Cl_{10}N_4Pd_2$	$C_{74}H_{94}Cl_4N_4O_8Pd_3$
FW	452.66	293.39	608.49	1498.70	1628.53
Color	yellow	colorless	colorless	orange	orange
Crystal size, mm^3	0.25 x 0.10 x 0.07	0.25 x 0.25 x 0.10	0.20 x 0.15 x 0.10	0.15 x 0.08 x 0.05	0.22 x 0.18 x 0.05
Crystal system	Orthorhombic	Monoclinic	Monoclinic	Monoclinic	Orthorhombic
Space group	Fdd2	C2/c	$P2_1/m$	$P\ 2_1/c$	Pnn2
a, Å	15.3632(15)	18.3891(6)	10.983(2)	12.5210(3)	13.101(3)
b, Å	41.9140(9)	14.9010(5)	14.196(3)	10.1820(2)	29.389(6)
c, Å	8.5520(9)	12.2811(4)	11.017(2)	27.5197(6)	10.898(2)
α, deg	90	90	90	90	90
β, deg	90	94.906(2)	106.04(3)	94.7006(8)	90
γ, deg	90	90	90	90	90
Z	8	8	2	2	2
ρ_{calc}, Mg m^{-3}	1.092	1.162	1.224	1.423	1.289
T, K	173(2)	173(2)	173(2)	173(2)	173(2)
$F(000)$	1968	1264	644	1536	1672
θ range, deg	3.65 to 25.02	3.52 to 26.37	2.40 to 27.48	2.29 to 27.48	2.80 to 25.35
Final $R_1(I > 2\sigma I)$	R1 = 0.0848, wR2 = 0.1899	R1 = 0.0478, wR2 = 0.1090	R1 = 0.0642, wR2 = 0.1563	R1 = 0.0510, wR2 = 0.0809	R1 = 0.0444, wR2 = 0.1106
R_1(all data)	R1 = 0.0973, wR2 = 0.1981	R1 = 0.0743, wR2 = 0.1242	R1 = 0.0815, wR2 = 0.1658	R1 = 0.0949, wR2 = 0.0954	R1= 0.0544, wR2 = 0.1167

2.4 Catalysis

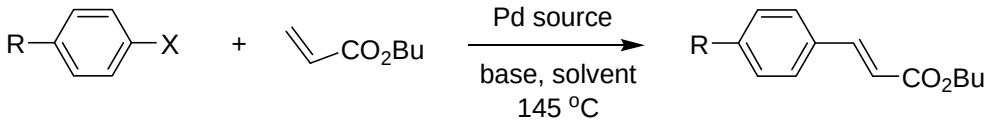
Cross-coupling reactions are powerful synthetic strategies to build carbon-carbon and carbon-heteroatom bonds.[42-44] Palladium catalyzed Heck and Suzuki coupling reactions are among the most efficient methods to construct C-C bonds.[45-50] The development of coupling

reactions for aryl chlorides has been a major research area in recent years as aryl chlorides tend to be cheaper and much more widely available than the analogous bromides or iodides but are however much more difficult to activate.[51] Along these lines, several powerful systems have been developed for the activation of not only aryl chlorides but alkyl halides as well.[52-59] While palladacycles have been around since 1965,[60] the first examples of palladacycles as precatalysts in the Heck and Suzuki reaction were not published until 1995.[61, 62] Palladacyclic compounds currently rank among the best catalysts for a variety of C-C coupling reactions.[61-65]

The catalytic activity of complexes **5** and **6** were investigated in the Heck coupling reaction of aryl halides with butylacrylate (Table 2.7). Complex **5** showed similar catalytic activity to that of ligand-free $PdCl_2$ suggesting the ligand plays little if any role in the catalytic cycle. This is not unexpected given the monodentate nature and poor sigma donating ability of the γ-diimine ligand. No activity was observed with aryl chlorides. Palladacycle **6** on the other hand, was a comparatively exceptional precatalyst even in the absence of stabilizing agents such as tetrabutylammonium iodide. Reactions were carried out in DMA at 145 °C in the presence of either CsOAc or Cs_2CO_3. The catalyst was active for both activated and deactivated aryl bromides (Table 2.7). Palladacycle **6** also demonstrated activity for aryl chlorides, however longer reaction time (24 h) was required. Palladacycle **6** was active for the coupling of butylacrylate with 4-chloroacetophenone (18%) and 4-chlorobenzaldehyde (99%).

The central palladium in **6** could serve as a source of catalytically active $Pd(OAc)_2$ thus the catalytic activity of **6** was compared to that of $Pd(OAc)_2$. Under the conditions employed, $Pd(OAc)_2$ showed no activity for the coupling of aryl chlorides. Under different conditions, $Pd(OAc)_2$ has been reported to be active for the coupling of aryl bromides and aryl chlorides.[66, 67]

Table 2.7. Heck Cross-Coupling of Aryl Halides with Butylacrylate [a].

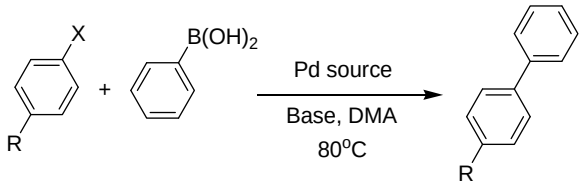


Entry	R	X	Base	Time (h)	Catalyst (mol %)	Conversion (%)[b]	TON[c]
1	H	I	Cs_2CO_3	3	**5** (0.1)	>99	1000
2	H	Br	Cs_2CO_3	3	**5** (1)	50	50
3	COMe	Br	CsOAc	14	**5** (1)	97	97
4	CN	Br	CsOAc	14	**5** (3)	86	29
5	Me	Br	Cs_2CO_3	3	**5** (1)	66	66
6	COMe	Cl	CsOAc	42	**5** (3)	0	0
7	COMe	Br	CsOAc	14	$PdCl_2$ (1)	>99	100
8	H	Br	Cs_2CO_3	3	$PdCl_2$ (1)	48	48
9	COMe	Br	CsOAc	3	**6** (0.01)	>99	10 000
10	COH	Br	Cs_2CO_3	3	**6** (0.1)	>99	1000
11	CN	Br	Cs_2CO_3	3	**6** (1)	88	88
12	OMe	Br	CsOAc	3	**6** (1)	65	65
13	Me	Br	CsOAc	24	**6** (1)	95	95
14	COH	Cl	Cs_2CO_3	24	**6** (1)	>99	100
15	COMe	Cl	CsOAc	6	**6** (1)	18	18
16	COMe	Cl	CsOAc	3	$Pd(OAc)_2$ (1)	0	0
17	COH	Cl	Cs_2CO_3	24	$Pd(OAc)_2$ (1)	0	0

[a]Reaction conditions: aryl halide (1.0 mmol), acrylate (2.0 mmol), base (2.0 mmol), Pd catalyst, solvent (DMA, 3 ml), 145 °C. [b]Determined by ^{1}H NMR based on residual aryl halide.[68-71] [c]TON = turnover number (mol product per mol catalyst).

The catalytic activity of complexes **5** and **6** were also tested in the Suzuki coupling reaction of aryl halides with phenylboronic acid, using Cs_2CO_3 or CsOAc as base and DMA as solvent at 80 ^oC (Table 2.8). As with the Heck reactions, while complex **5** was active for the catalytic coupling of aryl bromides, little or no activity was observed with aryl chlorides. Palladacycle **6** again demonstrated good activity for activated aryl chlorides producing the target biphenyls in 73-86 % yields, however lower yields were achieved for deactivated aryl chlorides (entries 7 and 11 in Table 2.8).

Table 2.8. Suzuki Cross-Coupling of Aryl Halides with Phenylboronic Acid[a].



Entry	R	X	Base	Time (h)	Catalyst (mol %)	Conversion (%)[b]
1	H	I	Cs_2CO_3	3	**5** (1)	>99
2	H	Br	Cs_2CO_3	3	**5** (1)	94
3	Me	Br	Cs_2CO_3	3	**5** (1)	92
4	COMe	Br	Cs_2CO_3	3	**5** (1)	98
5	COMe	Cl	Cs_2CO_3	3	**5** (3)	3
6	H	Cl	Cs_2CO_3	3	**5** (3)	0
7	OMe	Cl	Cs_2CO_3	24	**6** (1)	8
8	COH	Cl	Cs_2CO_3	24	**6** (1)	73
9	COMe	Cl	CsOAc	24	**6** (1)	86
10	CN	Cl	Cs_2CO_3	3	**6** (1)	78
11	Me	Cl	Cs_2CO_3	24	**6** (1)	17

[a]Reaction conditions: aryl halide (1.0 mmol), phenylboronic acid (1.5 mmol), Base (2 mmol), Pd catalyst (1 mol%), DMA (3 ml), 80 °C, 3 h. [b]Determined by ^1H NMR based on residual aryl halide.[24]

2.5 Conclusion

We have prepared and structurally characterized a bulky γ-diimine ligand and its corresponding Pd(II) complexes. Analogous γ-diimines are likely intermediates in the reaction of phthalaldehyde with primary amines to form the corresponding iminoisoindolines and isoindolinones due to rapid intramolecular cyclization reactions.[29-34] γ-Diimine **2** can however be isolated due to the presence of bulky diisopropylphenyl groups which likely inhibit or retard cyclization reactions. Depending on reaction conditions, cyclization of the γ-diimine can be induced to form either the corresponding iminoisoindoline or the isoindolinone. Unlike analogous α- and β-diimine complexes, the γ-diimine ligand does not coordinate in a chelating mode but instead adopts a monodentate coordination mode upon reaction with $PdCl_2$. On the other hand, reaction of γ-diimine **2** with $Pd(OAc)_2$ results in C-H activation of the ligand and formation of an air stable palladacyclic species containing a rare $Pd_3(OAc)_4$ core. The resulting palladacyclic complex is an active precatalyst for the Suzuki and Heck coupling reactions when para-functionalized aryl chlorides and aryl bromides are employed. The non-palladacyclic analogue, $[(\gamma\text{-diimine})PdCl(\mu\text{-}Cl)]_2$ is a relatively inferior precatalyst exhibiting no activity for aryl chlorides. Due to intramolecular cyclization reactions, it is unlikely that γ-diimines will emerge as a new class of ligand comparable to α- and β-diimine analogues.

2.6 Experimental Section

General Information. Unless otherwise stated, all reactions were performed under N_2 or vacuum using standard Schlenk techniques or in a N_2-filled drybox. All reaction temperatures for catalytic reactions refer to the temperature of pre-equilibrated oil or sand baths. All melting points were recorded on a Gallenkamp melting point apparatus and are uncorrected. ^1H and ^{13}C $\{^1H\}$ NMR

spectra were recorded on a Bruker 500 MHz Avance spectrometer. Chemical shifts for ^{1}H and ^{13}C NMR are reported in ppm in reference to the residual ^{1}H and ^{13}C resonances of $CDCl_3$ (^{1}H: δ 7.24; ^{13}C: δ 77.24). Coupling constants are given in Hz. High resolution mass spectra (HRMS) were measured on an Applied Biosystem QSTAR® XL MS/MS system (ESI-QTOF). Elemental analyses were performed on a Perkin-Elmer 2400 CHN elemental analyzer. IR data were collected by Diffuse Reflectance Spectroscopy. Reagents such as $PdCl_2$, $Pd(OAc)_2$, 2,6-diisopropylaniline, phthalaldehyde, and cyclooctene (COE) were purchased from Sigma-Aldrich Chemical Company and used as received except for 2,6-diisopropylaniline which was distilled prior to use. $(CH_3CN)_2PdCl_2$[72] and $[(COE)PdCl_2]_2$ [73] were synthesized according to literature procedures.

Synthesis of 1-phenylimino-2-phenylisoindoline.

A Schlenk flask was charged with phthalaldehyde (500 mg, 3.73 mmol), aniline (695 mg, 7.46 mmol), methanol (10 mL) and two drops of formic acid and stirred at ambient temperature for 12 h. The resulting precipitate was filtered and washed with methanol (3 x 20 mL), then dried under vacuum to obtained a white solid (510 mg, 48.5%, mp = 127.8 – 129.5ºC). ^{1}H NMR ($CDCl_3$, ppm) δ 8.01 (d, *J* = 6.0Hz, 2H), 7.44 (d, *J* = 7.5Hz, 1H), 7.38 (m, 3H), 7.31 (m, 2H), 7.04 (m, 3H), 6.99 (d, *J* = 6.7Hz, 2H), 6.66 (d, *J* = 7.1Hz, 1H), 4.94 (s, 2H); ^{13}C NMR ($CDCl_3$, ppm): δ 153.52, 150.87, 141.81, 140.59, 130.48, 129.34,129.12, 127.53, 126.70, 123.33, 122.92, 122.44, 121.44, 120.18, 53.18. Elemental analysis (%) calcd for $C_{20}H_{15}N_2$: C 84.48, H 5.67 , N 9.85; found: C 84.57, H 5.62, N 9.60.; MS (TOF) *m/z* calcd for $C_{20}H_{15}N_2$:284.1313; found: 285.1392 (M+1); FT-IR (KBr) = 1646 (C=N), 1590, 1498.

Synthesis of 2,5-dimethyl-1-(2,6-diisopropylphenyl)pyrrole (1).

A Schlenk flask was charged with 2,5-hexanedione (1.425 g, 0.0125 mol) and 2,6-disopropylaniline (6.65 g, 0.0375 mol), methanol (10 mL) and a drop of formic acid and stirred at ambient temperature for 12 h. The flask was then placed in a -30 ^{o}C freezer where colorless needle-like crystals formed. The solvent was decanted and the resulting product washed with cold methanol then dried under vacuum to yield a white powder of the title compound (2.03 g, 90%). ^{1}H NMR ($CDCl_3$): δ 7.39 (t, J = 7.7, 1H, C_6H_3), 7.61 (d, J = 7.7, 2H, C_6H_3), 5.92 (s, 2H, C_4H_2N), 2.35 (sept, J = 6.9, 2H, $CH(CH_3)_2$), 1.89 (s, 6H, $C_4H_2N(CH_3)_2$), 1.1 (d, J = 6.9, 12H, $CH(CH_3)_2$). ^{13}C NMR ($CDCl_3$): δ 147.8, 134.3, 129.3, 129.0, 124.0, 105.5, 28.0 ($CH(CH_3)_2$), 24.3 ($CH(CH_3)_2$), 12.9 (CH_3). Anal. Calcd for $C_{18}H_{25}N$: C 84.65; H 9.87; N 5.48. Found: C 84.41; H 9.60; N 5.45. EI-MS (*m/z*): calcd for $C_{18}H_{29}N$: 255.1987, found: 255.1985.

Synthesis of the γ-diimine 1,2-(2,6-^{i}Pr$_2$-C$_6$H$_3$NC)$_2$-C$_6$H$_4$ (2) and *N*-(2,6-diisopropylphenyl)isoindolinone (3).

A flask was charged with phthaldehyde (1.502 g, 11.2 mmol), 2,6-diisopropylaniline (14.1 g, 79.5 mmol) and methanol (15 mL) under nitrogen atmosphere. Formic acid (0.4 mL) was added and the mixture stirred at 0 ^{o}C. A yellow precipitate appeared within 10 min of stirring. After 4 h of stirring, the precipitate was filtered, washed with methanol (3x10 mL) and dried under vacuum to yield **2** as a yellow powder (3.371 g, 66%). Yellow crystals were obtained from slow evaporation of ether at ambient temperature. The colorless filtrate was transferred back to the flask where continued stirring was allowed for 12 h. Methanol and excess 2,6-diisopropylaniline were removed at 100 ^{o}C by vacuum distillation. Ether (10 mL) was added and the flask was placed in a -30 ºC freezer whereupon colorless crystals of **3** were obtained (0.985 g, 30%).

1,2-(2,6-$^{i}Pr_2$-$C_6H_3NC)_2$-C_6H_4 (2). ^{1}H NMR ($CDCl_3$): δ 8.82 (s, 2H, C=N*H*), 8.11 (dd, *J* = 5.7, 3.4, 2H, C_6H_4), 7.63 (dd, *J* = 5.7, 3.4, 2H, C_6H_4), 7.07 (m, 6H, 2,6-$^{i}Pr_2$-C_6H_3), 2.94 (sept, *J* = 6.6, 4H, C*H*$(CH_3)_2$), 1.08 (d, 24H, *J* = 6.9, CH(C*H*$_3)_2$). ^{13}C NMR ($CDCl_3$): δ 161.8, 149.8, 137.5, 135.9, 131.5, 130.3, 124.7, 123.4, 28.4 (*C*H), 24.9(*C*H_3). Anal. Calcd for $C_{32}H_{40}N_2$: C 84.90; H 8.90; N 6.18. Found: C 84.30; H 8.61; N 6.02. mp: 180.0-182.5 °C. FT-IR (KBr, cm^{-1}): 1633 (C=N). EI-MS (*m/z*): calcd for $C_{32}H_{40}N_2$: 452.3191; found: 452.3185.

Alternative synthesis of *N*-(2,6-diisopropylphenyl)isoindolinone (3).

A flask was charged with phthalaldehyde (0.526 g, 3.92 mmol), 2,6-diisopropylaniline (0.696 g, 3.92 mmol), formic acid (0.032 g, 0.695 mmol) and methanol (10 mL). After 19 h of stirring at ambient temperature, the flask was placed in a -30 °C freezer, whereupon colorless needle-like crystals formed. The solvent was decanted and the crystals dried under vacuum to yield a white powder of the title compound (0.861 g, 75%), mp = 155.0-157.0 ºC. ^{1}H NMR ($CDCl_3$): δ 7.98 (d, *J* = 7.5, 1H, C_6H_4), 7.61 (m, 1H, C_6H_4), 7.53 (d, *J* = 7.5, 1H, C_6H_4), 7.50 (d, *J* = 7.5, 1H, C_6H_4), 7.39 (t, *J* = 7.7, 1H, C_6H_3), 7.25 (d, *J* = 7.7, 2H, C_6H_3), 4.56 (s, 2H, CH_2), 2.76 (sept, *J* = 6.9, 2H, C*H*$(CH_3)_2$), 1.19 (d, *J* = 6.9, 12H, CH(C*H*$_3)_2$). ^{13}C NMR ($CDCl_3$): δ 168.8 (C=O), 147.8, 141.6, 133.0, 132.6, 131.8, 129.4, 128.5, 124.8, 124.3, 123.1, 54.0, 29.0 (*C*H), 24.7 (*C*H_3), 24.5 (*C*H_3). Anal. Calcd for $C_{20}H_{23}NO$: C 81.87; H 7.90; N 4.77. Found: C 81.70; H 7.80; N 4.76. FT-IR (KBr, cm^{-1}): 1694.8 (C=O). EI-MS (*m/z*): calcd for $C_{20}H_{23}NO$: 293.1779; found: 293.1774.

Synthesis of *N*,*N'*-bis(2,6-diisopropylphenyl)iminoisoindoline (4).

A flask was charged with γ-diimine **2** (100 mg, 0.220 mmol) and chloroform-d (10 mL). After 48 h of stirring at 60 ^{o}C under ambient atmosphere, the color of the solution had changed from yellow to colorless. The solvent was removed under vacuum to yield a white powder (91 mg, 91%). The cyclization was observed to proceed considerably slower when the reaction was performed under nitrogen in place of air. ^{1}H NMR ($CDCl_3$): δ 7.37 (m, 3H), 7.26 (d, *J* = 2, 2H), 7.05 (m, 4H), 6.38 (d, *J* = 8.0, 1H), 4.69 (s, 2H, C*H*$_2$), 3.19 (sept, *J* = 6.8, 2H, C*H*(CH_3)$_2$), 3.10 (sept, *J* = 6.8, 2H, C*H*(CH_3)$_2$), 1.32 (d, *J* = 6.8, 6H, CH(C*H*$_3$)$_2$), 1.23 (d, *J* = 6.8, 6H, CH(C*H*$_3$)$_2$), 1.07 (d, *J* = 6.9, 6H, CH(C*H*$_3$)$_2$), 0.87 (d, *J* = 6.9, 6H, CH(C*H*$_3$)$_2$). ^{13}C NMR ($CDCl_3$): δ 155.0, 147.88, 146.26, 140.97, 139.21, 134.47, 131.42, 129.75, 128.56, 127.15, 126.44, 124.09, 122.64, 122.27, 55.22, 28.44, 27.44, 25.81, 24.17, 23.62, 23.52. FT-IR (KBr, cm^{-1}): 1644 (C=N). EI-MS (*m/z*): calcd for $C_{32}H_{40}N_2$: 452.3191; found: 452.3185.

NMR tube reaction for the cyclization of γ-diimine 2 to iminoisoindoline 4.

An NMR tube was charged with **2** (3 mg, 6.6 μmol) and $CDCl_3$ (0.6 mL) under air. The reaction was monitored over 24 h at 60 ^{o}C. During the course of the reaction, the solution changed from yellow to colorless. ^{1}H NMR spectra showed complete conversion of **2** to **4** after 24 h. Prolonged exposure of **4** to $CDCl_3$ over the course of two weeks resulted in precipitation of colorless crystals of the DCl salt of **4** (**4·DCl**).

Cyclization of γ-diimine 2 to form *N*-(2,6-diisopropylphenyl)isoindolinone (3).

A flask was charged with **2** (28.00 mg, 0.0619 mmol), methanol (15 mL) and two drops of formic acid. After stirring for 24 h, the color of the solution changed from yellow to colorless.

Solvent was removed under vacuum and ^{1}H NMR analysis showed the quantitative conversion of **2** to **4** and along with formation of one equiv 2,6-diisopropylaniline.

Synthesis of [(γ-diimine)PdCl(μ-Cl)]$_2$ (5).

A Schlenk flask was charged with **2** (0.168 g, 0.371 mmol), $(CH_3CN)_2PdCl_2$ (0.053 g, 0.204 mmol) and benzene (20 mL) under nitrogen. Within 0.5 h of stirring at ambient temperature, the yellow-green mixture became a red-brown homogeneous solution. After 16 h, the resulting yellow-brown precipitate was filtered and washed with cold benzene (3x10 ml) under air. The product was then crystallized by slow evaporation from $CHCl_3$ to give orange crystals of **5** (0.121 g, 47%, mp = 181.5 – 182.0 ºC (decomp)). ^{1}H NMR ($CDCl_3$): 9.69 (d, *J* = 7.4Hz, 2H), 8.25 (s, 2H, *H*C=N), 8.17 (s, 2H, *H*C=N), 8.04 (t, *J* = 7.5Hz, 2H), 7.86 (m, 2H), 7.64 (d, *J* = 7.4Hz, 2H), 7.17 (t, *J* = 7.5Hz, 2H), 7.04 (d, *J* = 7.6Hz, 4H, C_6H_3), 7.00 (br, 6H), 3.26 (m, 4H, C*H*$(CH_3)_2$), 2.57 (m, 4H, C*H*$(CH_3)_2$), 1.64 (br, 9H, CH(C*H*$_3)_2$). 0.88-0.80 (m, 39H, CH(C*H*$_3)_2$). ^{13}C NMR ($CDCl_3$): δ 176.0, 161.8, 148.8, 145.9, 142.8, 137.6, 135.8, 133.8, 132.9, 132.8, 131.9, 130.4, 128.7, 125.1, 124.6, 123.3, 28.9, 28.4, 23.9, 23.8. FT-IR (KBr, cm^{-1}): 1633 (free imine, C=N), 1618 (Coordinated imine, C=N-Pd).

Synthesis of {1,2-(2,6-^{i}Pr$_2$-C$_6$H$_3$NC)$_2$-C$_6$H$_3$]Pd(μ-OAc)$_2$}$_2$Pd (6).

A Schlenk flask was charged with **2** (657 mg, 1.45 mmol), $Pd(OAc)_2$ (362 mg, 1.45 mmol) and ether (20 mL) under nitrogen. After 16 h of stirring at ambient temperature, the resulting orange precipitate was filtered in air and washed with cold ether (3x10 mL) and dried under vacuum. Orange crystals of **6** were obtained from dichloromethane/hexanes (1:1) by slow evaporation at ambient temperature (504 mg, 24%. mp = 206.5 – 208.5 °C (decomp)). ^{1}H NMR

($CDCl_3$): 9.50 (s, 2H, *H*C=N), 8.09 (s, 2H, *H*C=N), 7.44 (dd, *J* = 6.3, 2.5 Hz, 2H) 7.30 (m, 4H), 7.19 (m, 4H), 7.05 (m, 8H), 4.17 (sep, *J* = 7.0Hz, 2H, C*H*(CH_3)$_2$), 3.51 (sept, *J* = 7.0Hz, 2H), 2.84 (sept, 4H, C*H*(CH_3)$_2$), 1.98(s, 6H, OAc), 1.44(d, *J* = 7Hz, 6H, CH(C*H*$_3$)$_2$), 1.15(d, *J* = 7Hz, 6H, CH(C*H*$_3$)$_2$) 1.14(s, 6H, OAc), 1.05(d, *J* = 7Hz, 12H, CH(C*H*$_3$)$_2$) 1.04(d, *J* = 7Hz, 18H, CH(C*H*$_3$)$_2$), 1.01(d, J = 7Hz, 6H, CH(C*H*$_3$)$_2$). ^{13}C NMR ($CDCl_3$): δ 184.1, 183.0, 177.7, 162.6, 161.0, 148.9, 144.6, 143.6, 143.0, 141.8, 137.5, 135.5, 134.7, 130.7, 130.0, 127.6, 124.6, 123.3, 123.3, 123.2, 66.1, 28.5, 28.2, 27.8, 26.2, 24.8, 23.8, 23.6, 23.5, 23.5, 23.0, 22.9, 22.8, 15.5. Anal. calcd for $C_{72}H_{90}N_4O_8Pd_3$: C 59.28, H 6.22, N 3.84; found: C 58.89, H 6.44, N 3.71. FT-IR (KBr, cm^{-1}): 1631 (free imine, C=N), 1580 (Coordinated imine, C=N-Pd).

General procedure for the Heck coupling reactions

In a typical run, an oven-dried 25 mL two-necked flask equipped with a stir bar was charged with a known mol % catalyst and base (2.0 mmol). Under nitrogen, DMA (3 mL), aryl halides (1.0 mmol) and n-butylacrylate (2.0 mmol) were added via syringe. The flask was then placed in a pre-heated sand bath at 145 ^{o}C. After the specified time the flask was removed from the sand bath and water (20 mL) added followed by extraction with dichloromethane (4x10 mL). The combined organic layers were washed with water (3x10 mL), dried over anhydrous $MgSO_4$, and filtered. Solvent was removed under vacuum. The residue was dissolved in $CDCl_3$ and analyzed by ^{1}H NMR. Percent conversions were determined against the remaining aryl halide.[24]

General procedure for the Suzuki coupling reactions

In a typical run, an oven dried 25 mL two-necked flask equipped with a stir bar was charged with a known mol % catalyst, base (2.0 mmol) and phenylboronic acid (1.5 mmol). Under nitrogen, DMA (3 mL) and aryl halides (1.0 mmol) were added via syringe. The flask was

placed in pre-heated sand bath at 80 ^{o}C. After the specified time the flask was removed from the sand bath and water (20 mL) added followed by extraction with dichloromethane (4x10 ml). The combined organic layers were washed with water (3x10 mL), dried over anhydrous $MgSO_4$, and filtered. Solvent was removed under vacuum. The residue was dissolved in $CDCl_3$ and analyzed by ^{1}H NMR. Percent conversions were determined against the remaining aryl halide.[24]

X-ray structure determinations

Data were collected at -100°C on a Nonius Kappa CCD diffractometer, using the COLLECT program.[74] Cell refinement and data reductions used the programs DENZO and SCALEPACK.[75] SIR97[76] was used to solve the structures and SHELXL97[77] was used to refine the structures. ORTEP-3 for Windows[78] was used for molecular graphics and PLATON[79] was used to prepare material for publication. H atoms were placed in calculated positions with U_{iso} constrained to be 1.5 times U_{eq} of the carrier atom for methyl protons and 1.2 times U_{eq} of the carrier atom for all other hydrogen atoms.

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2.7 Supporting Information Available:

Full crystallographic data for compounds **2**, **3**, **4-DCl·CDCl$_3$**, **5·2CHCl$_3$** and **6·2CH$_2$Cl$_2$** are available as CIF files. This material is available free of charge via the Internet at http://pubs.acs.org.

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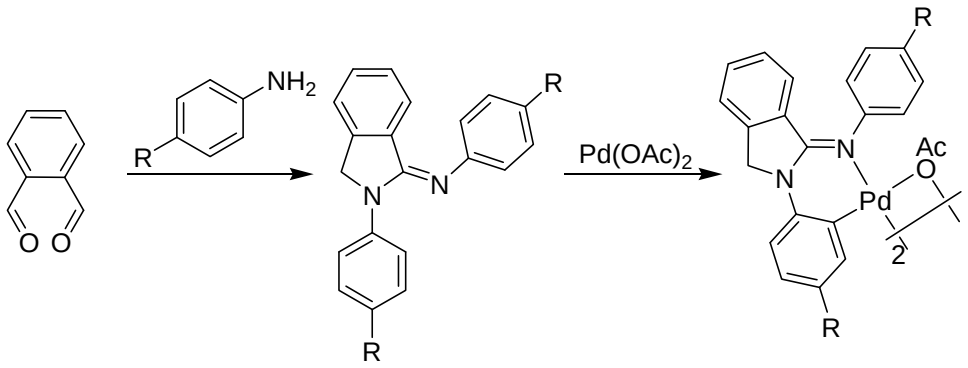
CHAPTER 3

PUBLICATION 2

Description

The following is a verbatim copy of an article published in September 2008 in a Royal Society of Chemistry Journal (*Dalton Trans*, **2008**, 6023-6029) and describes the synthesis of a series of air- and moisture-stable six-membered iminoisoindoline-based palladacycles of the general formula [(iminoisoindoline)Pd{μ-OAc}]$_2$ (**6-9**), which were prepared in a simple two-step protocol from commercially available starting materials. The dinuclear cyclopalladated complexes were tested as precatalysts for Suzuki and Heck C-C coupling reactions.



Authors' Contribution

I synthesized and fully characterized all five iminoisoindoline ligands (**1-5**) along with four of their corresponding iminoisoindoline-based palladacycles (**6-9**). I also conducted some Suzuki and Heck C-C coupling reactions using **6**. Demyan E. Prokopchuk, for his summer project, conducted some of the catalytic studies employing palladacycle **9**. J. Wilson Quail did all

the structure determination by single crystal X-ray analysis and the work was supervised by Stephen R. Foley.

Relation of Chapter 3 (Publication 2) to the overall Objectives of this Project

As mentioned in Chapter 2, when the only isolated γ-diimine (with 2,6-diisopropylaniline) was treated with $Pd(OAc)_2$, a five-membered palladacycle instead of a seven-membered palladium coordination complex was obtained. In addition, reaction of *o*-phthaladehyde with less bulky anilines than 2,6-diisopropylaniline gave iminoisoindolines as products rather than γ-diimines. Diaryliminoisoindolines appeared to be good ligand systems for the formation of iminoisoindoline-based palladacycles. Furthermore, in the literature, palladacycles are among the most active precatalysts for C-C coupling reactions. Consequently, this chapter looks at the synthesis of a series of six-membered iminoisoindoline-based palladacycles for C-C coupling reactions.

3. Synthesis of Palladacycles employing Iminoisoindolines as Monoanionic Bidentate Ligands

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3.1 Abstract

A series of air and moisture stable iminoisoindoline-based palladacycles have been prepared in two operationally simple steps from commercially available reagents. *Para*-substituted N,N'-diphenyliminoisoindoline ligands are easily synthesized from phthalaldehyde and *para*-substituted anilines and further reaction of the iminoisoindoline ligands with $Pd(OAc)_2$ in dichloromethane at room temperature results in formation of six-membered [C,N] dinuclear cyclopalladated complexes with the general formula $[(iminoisoindoline)Pd\{\mu\text{-}OAc\}]_2$. The resulting palladacyclic complexes were tested as precatalysts in Heck and Suzuki coupling reactions.

3.2 Introduction

Palladacycles represent an increasingly important class of organometallic compounds, where their influence is especially dominant in the field of coupling reactions for organic transformations.[1-4] This is reflected in the diversity of the palladacycles that have been reported in

literature, most common of which are palladacycles incorporating [C,P] and [C,N] metallacycle formations.[5-10] Many palladium-mediated coupling reactions are thought to involve palladacyclic intermediates[11] and several palladacycles are also reported to be biologically active compounds for cancer therapy.[12, 13] The majority of palladacycles contain one σM-C_{sp^2} or σM-C_{sp^3} bond in a chelating bidentate monoanionic ligand environment, with five- or six-membered N- or P-containing ring systems.[5-10]

We previously reported the synthesis of a γ-diimine ligand in which intramolecular cyclization could be induced to form the corresponding iminoisoindoline.[14] Upon reaction of the γ–diimine with $Pd(OAc)_2$, a five-membered palladacycle was synthesized. With this in mind, we thought that iminoisoindoline ligands could represent a convenient and facile route into the formation of rare [C,N] imine-based six-membered palladacycles. Iminoisoindolines could coordinate to palladium through the imine functionality, followed by C-H activation of the N-bound aryl group and subsequent *ortho*-palladation. There are several examples of tridentate [N,N,N] and [C,N,N] iminoisoindolines as ligands in pincer-type complexes,[15-22] however we describe here the first synthesis and characterization of palladacyclic species derived from monoanionic bidentate [C,N] iminoisoindoline ligands.

A wide variety of *para*-substituted iminoisoindoline ligands can be prepared in a one pot procedure from commercially available starting materials involving simple condensation reactions of phthalaldehyde and *para*-substituted anilines (Figure 3.1). The ligands precipitate from the reaction mixture as analytically pure solids. Palladacyclic complex formation is also facile, simply involving reaction of the iminoisoindoline ligand with $Pd(OAc)_2$ resulting in precipitation of the desired palladacyclic species as air and moisture stable orange or green solids. Here we present a simple two step procedure for the synthesis of four iminoisoindoline-based

palladacycles from commercially available starting materials. The catalytic activities of this new family of palladacycles were tested in standard Heck and Suzuki coupling reactions.

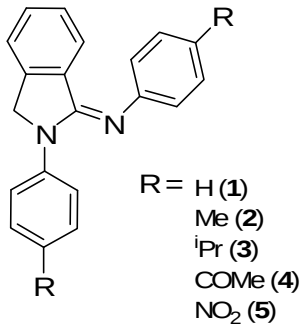


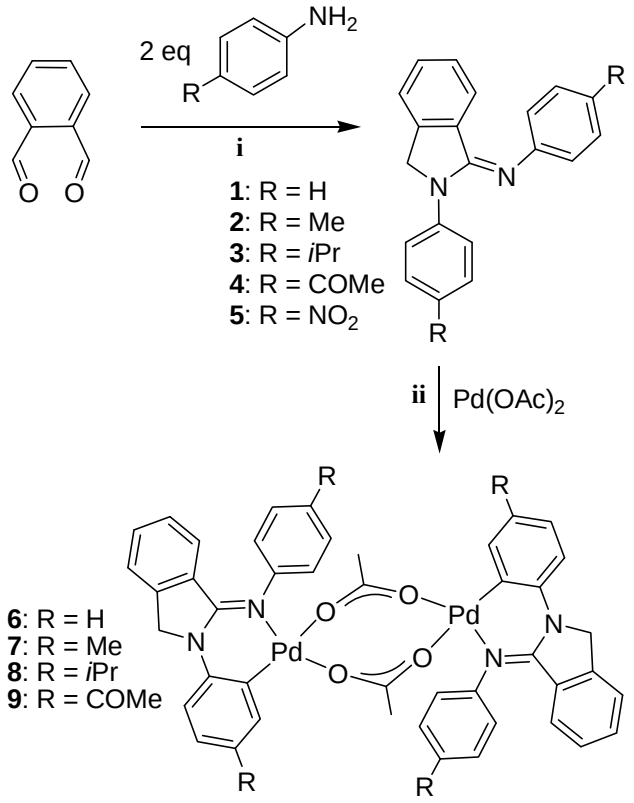
Figure 3.1. Iminoisoindoline ligands

3.3 Results and discussion

Iminoisoindoline ligands **1-5** were prepared by the reaction of phthalaldehyde with 2 equiv of the corresponding aryl amine under dinitrogen in high yield according to Scheme 3.1. The particular ligands were chosen in order to investigate electronic and steric effects in the *para* positions of the N-aryl substituents (R = H (**1**), Me (**2**), ^{i}Pr (**3**), COMe (**4**), NO_2 (**5**); Scheme 1). The iminoisoindoline ligands precipitate from solution as analytically pure white or yellow solids. Except for **3**, the iminoisoindolines have all been previously reported, however their potential as ligands has never before been investigated.[23, 24]

It has been previously proposed that *in-situ* formation of a γ–diimine followed by rapid intramolecular cyclization results in formation of the corresponding iminoisoindoline.[23-28] We have recently reported that a γ–diimine can be isolated, provided sufficient steric bulk is

introduced in the *ortho* positions of the aryl-N substituent to retard cyclization. Even then, the γ–diimine was observed to undergo slow cyclization in the presence of catalytic amounts of H^+.[14]



Scheme 3.1. Preparation of iminoisoindoline ligands and their corresponding palladacycles. (i) ether, 12 h, RT, (ii) dichloromethane, 12 h, RT

3.3.1 Synthesis of [(iminoisoindoline)Pd{μ-OAc}]$_2$ palladacycles

Cyclopalladated complexes **6-9** were obtained by reaction of $Pd(OAc)_2$ with one equiv of the respective iminoisoindoline **1-4** in dichloromethane at ambient temperature yielding the desired palladacycles, of the general formula [(iminoisoindoline)Pd(μ-OAc)]$_2$, as analytically pure precipitates (Scheme 3.1). Interestingly, no reaction was observed with NO_2-substituted iminoisoindoline **5** and $Pd(OAc)_2$. This is likely due to the electron withdrawing/deactivating

effects of the nitro substituent inhibiting both imine coordination and *ortho*-palladation. Complexes **6-9** are air and moisture stable complexes that decompose above 200 ºC. No coordination complexes were observed prior to cyclopalladation. Palladacycles **6-9** were characterized by IR and NMR spectroscopy, mass spectrometry and elemental analysis. Crystal structures were obtained for complexes **6-9**.

The IR data confirmed the presence of the Pd-N bond in the cyclopalladated complexes. In the spectra of complexes **6-9**, the signals for the C=N bond vibrations were shifted to lower wavenumber compared to those of the free iminoisoindoline (Δ(wavenumber) ~ 35 cm^{-1}).

Dinuclear palladacycles in which the two palladium centers are linked by two bridging acetato groups can exhibit *anti*- and *syn*-isomerization (Figure 2).[29-34] In this case, NMR data allows for easy differentiation between the *anti*- and *syn*-conformations where the *anti*-isomer exhibits overall C_2 symmetry and the *syn*-isomer is C_s symmetric. A characteristic indication of cyclopalladation in complexes **6-9** is the observed ^{1}H NMR resonance for the CH_2 protons of the iminoisoindoline ring. The ligands (**1-5**) show a singlet corresponding to the two methylene protons at ~5 ppm. Upon cyclopalladation, these methylene protons become diastereotopic in the *anti*-isomer resulting in formation of two doublets at ~4.6 and ~3.5 ppm, each corresponding to one proton per ligand. The *syn*-isomer, on the other hand, shows a singlet for the methylene protons shifted slightly downfield (~0.1 ppm) relative to that of the free ligand. Due to steric effects, the *anti*-isomer is favored over the *syn*-isomer with *anti/syn* ratios increasing as the steric bulk in the *ortho* position of the iminoisoindoline ring increases. Thus, *anti/syn* isomers were observed in ratios from 8:1 for **9** (R = COMe) to 3:1 for **6** (R = H). The mass spectra of complexes **6-9** all showed a distinct signal which was assigned to their respective molecular cation $[M\text{-}OAc]^+$.

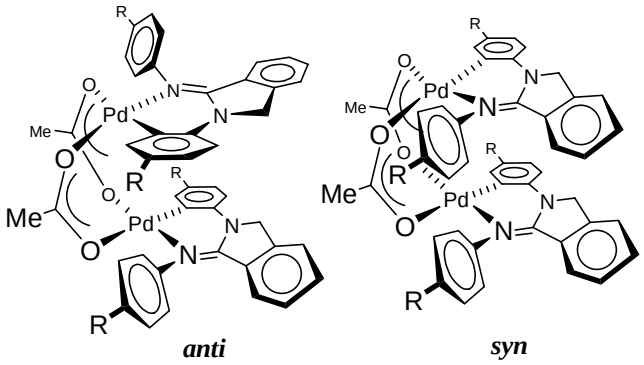


Figure 3.2. Isomers of [(iminoisoindoline)Pd(μ-OAc)]$_2$ (**6**-**9**)

The crystal structures of palladacycles **6**-**9** were determined. All four structures co-crystallized with one molecule of the solvent from which they were grown. Complexes **6** and **9** co-crystallized with one molecule of dichloromethane, while **7** co-crystallized with one molecule of chloroform and **8** co-crystallized with one molecule of acetone. All four complexes crystallized exclusively as the *anti*-isomer, unambiguously confirming the presence of a six-membered [C,N] palladacycle. The *anti*-configuration is also observed in the crystal structures of previously reported acetato-bridged dinuclear palladacycles,[29-34] with the exception of one report showing the exclusive crystallization of a *syn*-isomer.[35] The two palladium atoms in **6**-**9** are bridged by two acetate ligands and each palladium center has a chelating [C,N]-bound iminoisoindoline ligand forming the palladacycle. The dinuclear acetato-bridged complexes adopt a characteristic closed-book conformation where the two [C,N]-bound iminoisoindoline ligands stack on top of one another. As expected, the coordination geometry about the palladium atoms in all three structures is approximately square planar with the sum of the angles around the palladium atoms for all three complexes being 360±1°. The Pd-Pd distance was found to be 2.9975(4) Å for **6**, 3.0049(3) Å for **7**, 3.1130(3) for **8** and 2.9685(6) Å for **9** which is consistent with previously reported acetato-bridged dinuclear palladacycles.[29-34] The Pd-C and Pd-N bond lengths of complexes **6**-**9**

were all essentially identical (within esd) at 1.97(1) Å and 2.01(1) Å respectively. The Pd–O distances of the two acetate ligands differ by about 0.10 Å for **6-9** (for example, in **6**, Pd(1)-O(1) is 2.157 Å while Pd(1)-O(3) is 2.053 Å), indicative of the stronger trans-influence of the aryl carbon compared to that of the imine nitrogen.

ORTEP plots for **6-9** shown in Figures 3.3 through 3.6 with bond distances and angles indicated in their respective captions. Crystallographic data are summarized in Table 3.1.

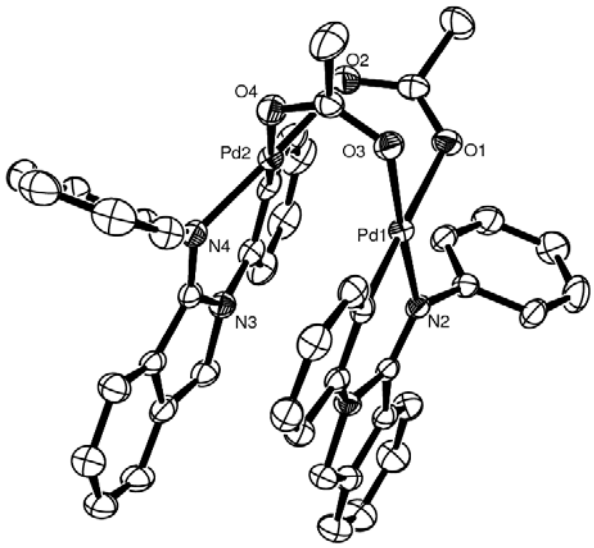


Figure 3.3. ORTEP plot of **6** at the 50% probability level. The hydrogen atoms have been omitted for clarity. Selected bond lengths [Å] and angles [^{o}]: Pd(1)-C(10) = 1.972(3), Pd(1)-N(2) = 2.004(3), Pd(1)-O(3) = 2.053(3), Pd(1)-O(1) = 2.157(2), Pd(1)-Pd(2) = 2.9975(4), C(10)-Pd(1)-N(2) = 90.40(13), C(10)-Pd(1)-O(3) = 91.70(13), N(2)-Pd(1)-O(1) = 95.31(10), O(3)-Pd(1)-O(1) = 82.46(10)

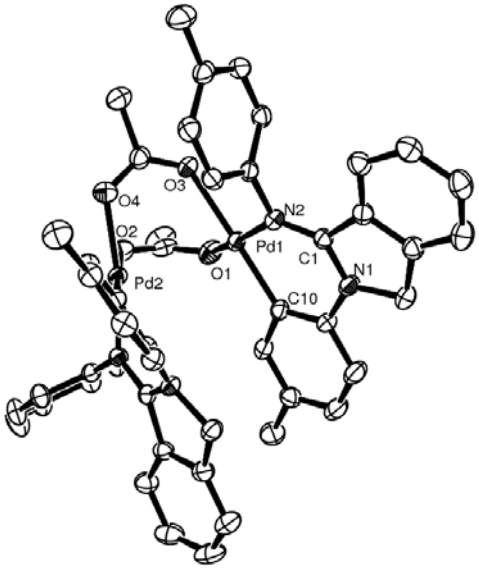


Figure 3.4. ORTEP plot of **7** at the 50% probability level. The hydrogen atoms have been omitted for clarity. Selected bond lengths [Å] and angles [^{o}]: Pd(1)-C(10) = 1.969(3), Pd(1)-N(2) = 2.016(3), Pd(1)-O(3) = 2.159(2), Pd(1)-O(1) = 2.083(2), Pd(1)-Pd(2) = 3.0049(3), C(10)-Pd(1)-N(2) = 90.00(11), N(2)-Pd(1)-O(3) = 93.85(9), C(10)-Pd(1)-O(1) = 91.77(11), O(3)-Pd(1)-O(1) = 84.22(9)

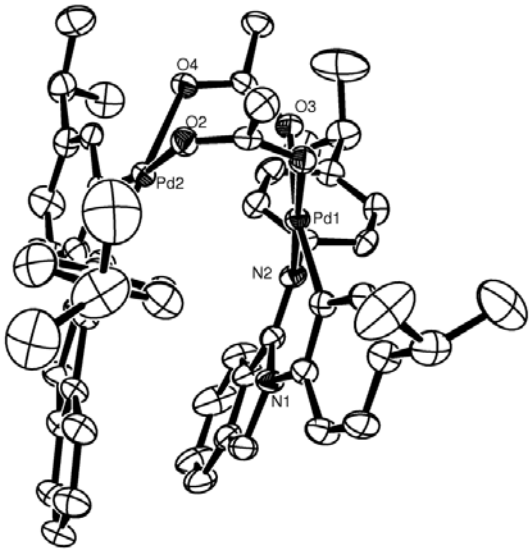


Figure 3.5. ORTEP plot of **8** at the 30% probability level. The hydrogen atoms have been omitted for clarity. Selected bond lengths [Å] and angles [^{o}]: Pd(1)-C(10) = 1.960(3), Pd(1)-N(2) = 2.004(3), Pd(1)-O(3) = 2.139(2), Pd(1)-O(1) = 2.055(2), Pd(1)-Pd(2) = 3.1130(3), C(10)-Pd(1)-N(2) = 88.62(12), C(10)-Pd(1)-O(1) = 89.63(11), N(2)-Pd(1)-O(3) = 93.95(10), O(3)-Pd(1)-O(1) = 87.84(9)

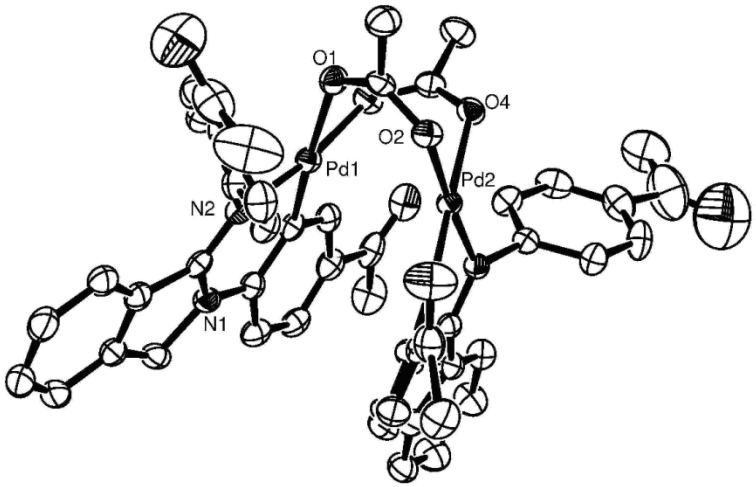


Figure 3.6. ORTEP plot of **9** at the 50% probability level. The hydrogen atoms and CH_2Cl_2 have been omitted for clarity. Selected bond lengths [Å] and angles [^{o}]: Pd(1)-C(10) = 1.975(5), Pd(1)-

N(2) = 2.008(4), Pd(1)-O(3) = 2.064(4), Pd(1)-O(1) = 2.147(4), Pd(1)-Pd(2) = 2.9685(6), C(10)-Pd(1)-N(2) = 90.7(2), C(10)-Pd(1)-O(3) = 92.70(19), N(2)-Pd(1)-O(1) = 94.02(16), O(3)-Pd(1)-O(1) = 82.65(15)

Table 3.1. Crystal data and refinement parameters for complexes **6-9**.

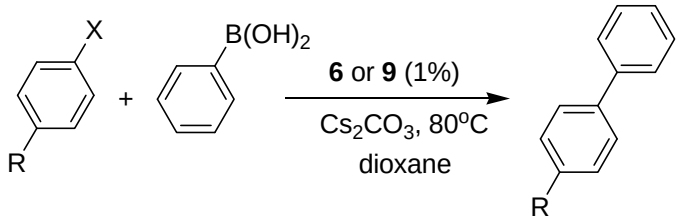
	6·CH_2Cl_2	**7·$CHCl_3$**	**8·$CO(CH_3)_2$**	**9·CH_2Cl_2**
formula	$C_{45}H_{38}Cl_2N_4O_4Pd_2$	$C_{49}H_{45}Cl_3N_4O_4Pd_2$	$C_{59}H_{66}N_4O_5Pd_2$	$C_{54}H_{46}Cl_2N_4O_8Pd_2$
formula wt	982.49	1073.04	1123.96	1150.64
color	green	orange	yellow	orange
crystal system	monoclinic	monoclinic	monoclinic	monoclinic
space group	$P2_1/c$	$P2_1/c$	$P2_1/c$	$P2_1/c$
a, Å	12.5421(2)	23.1864(3)	13.7107(2)	18.6888(8)
b, Å	16.7665(3)	9.6437(1)	19.1758(3)	13.9845(11)
c, Å	18.9026(4)	20.2415(2)	21.3745(3)	21.6903(11)
α, deg	90	90	90	90
β, deg	91.3617(13)	105.026(1)	106.88830(10)	124.159(3)
γ, deg	90	90	90	90
Z	4	4	4	4
ρ_{calc}, Mg m^{-3}	1.642	1.630	1.388	1.629
temp, K	173(2)	173(2)	173(2)	173(2)
F(000)	1976	2168	2320	2328
θ range, deg	2.47 to 26.37	2.35 to 28.71	2.26 to 27.47	2.63 to 25.35
final R_1(I >2σI)	R1 = 0.0384, wR2 = 0.0830	R1 = 0.0403, wR2 = 0.0809	R1 = 0.0426, wR2 = 0.0878	R1 = 0.506, wR2 = 0.1144
R_1(all data)	R1 = 0.0556, wR2 = 0.0924	R1 = 0.0615, wR2 = 0.0889	R1 = 0.0696, wR2 = 0.1004	R1 = 0.695, wR2 = 0.1247

3.4 Catalysis

While palladacycles have been around since 1965,[36] the first examples of palladacycles as precatalysts in the Heck and Suzuki reaction were not published until 1995.[37] Palladacyclic compounds currently rank among the best precatalysts for a variety of C-C coupling reactions.[1, 37] Several palladacycles are now commercially available from chemical companies such as Aldrich and Strem and most notably include the imine-based Nájera catalyst,[38] the amine-based Indolese catalyst[39] and Bedford's phosphite-based catalyst.[40]

The catalytic activity of palladacyclic complexes **6** and **9** was tested in the standard Suzuki coupling reaction of aryl halides with phenylboronic acid, using Cs_2CO_3 as a base, 1% precatalyst loading and dioxane as solvent at 80 ºC under dinitrogen. As shown in Table 3.2, good to excellent yields of biphenyls were obtained in the Suzuki coupling reaction for both activated and deactivated aryl bromides. Interestingly, for activated aryl chlorides, **6** gave only a 43% yield (entry 6), while **9** resulted in quantitative yields (entries 13 and 14). With deactivated chlorides however, low conversions were obtained.

Table 3.2. Suzuki Cross-Coupling of Aryl Halides with Phenylboronic Acid.[a]



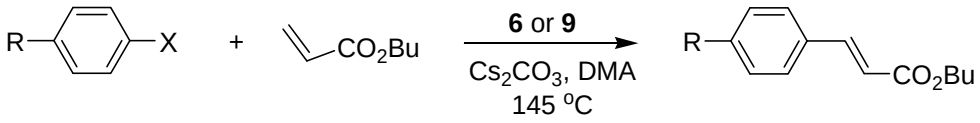
Entry	R	X	time (h)	Cat.	Conv. (%)*
1	H	I	3	**6**	>99
2	H	Br	3	**6**	94
3	Me	Br	3	**6**	92
4	COMe	Br	3	**6**	75
5	CN	Br	3	**6**	80
6	COMe	Cl	18	**6**	43
7	Me	Br	24	**9**	94
8	CN	Br	24	**9**	>99
9	COMe	Br	24	**9**	>99
10	OMe	Br	24	**9**	90
11	OMe	Cl	96	**9**	18
12	Me	Cl	24	**9**	27
13	COMe	Cl	24	**9**	>99
14	CN	Cl	24	**9**	>99

[a]Reaction conditions: 1mmol of aryl halides, 1.5 mmol phenyl boronic acid, 2 mmol Cs_2CO_3, 1 mmol % Pd precatalyst, 3 mL of dioxane. *Determined by ^{1}H NMR in reference to the residue aryl-halide.[39, 40]

We further investigated the activity of palladacyclic complexes **6** and **9** in the standard Heck reaction of activated and deactivated aryl halides with butyl acrylate. The results are shown

in Table 3.3. Quantitative yields were obtained when employing bromoanisole and bromobenzaldehyde in the presence of 0.01 and 0.1 mol% of **9** respectively (entries 5 and 6), even at lower temperature (100 ºC, entry 7). A decrease in activity was observed when deactivated aryl bromides such as *p*-bromotoluene (61%) and *p*-bromoanisole (56%) were used. Among the activated aryl chlorides only chlorobenzaldehyde and bromobenzonitrile gave a fairly good conversion of 60% and 53% respectively, while *p*-acetochlorobenzene resulted in only 16% conversion (entry 11). Under the same conditions, coupling of deactivated aryl chlorides was unsuccessful.

Table 3.3. Heck Cross-Coupling of Aryl Halides with Butyl Acrylate. [a]



Entry	R	X	time (h)	catalyst (mol %)	conversion (%)[b]	TON[c]
1	H	I	3	**6** (0.001)	>99	100000
2	H	Br	3	**6** (1)	71	71
3*	H	Cl	12	**6** (3)	0	0
4	CN	Br	3	**9** (1)	96	96
5*	COMe	Br	3	**9** (0.01)	>99	10000
6	COH	Br	3	**9** (0.1)	>99	1000
7**	COH	Br	24	**9** (1)	>99	100
8	Me	Br	3	**9** (1)	61	61
9	OMe	Br	3	**9** (1)	56	56
10	COH	Cl	3	**9** (1)	60	60
11*	COMe	Cl	24	**9** (1)	16	16
12	CN	Cl	24	**9** (1)	53	53

[a]Reaction conditions: aryl halide (1.0 mmol), acrylate (2.0 mmol), base (2.0 mmol), Pd precatalyst, solvent (DMA, 3 ml), 145 °C. [b]Determined by ^{1}H NMR based on residual aryl halide.[39, 40] [c]TON = turnover number (mol product per mol catalyst). *CsOAc used as base. **Performed at 100 °C.

3.5 Conclusion

We have synthesized and studied a series of air and moisture stable iminoisoindoline-based palladacycles. These complexes are easily prepared in two operationally simple steps from commercially available reagents. Complexes **6** and **9** were found to be active precatalysts for the Suzuki and Heck C-C coupling reactions with precatalyst **9** (R = COMe) exhibiting significantly higher activity than **6** (R = H). If highly electron withdrawing groups are employed on the diphenyliminoisoindoline ligands (i.e. iminoisoindoline **5**, R = NO_2), palladacyclic formation is completely inhibited. Further investigations on the reactivity and catalytic activity of this family of palladacycles are underway and this work will be reported at a later date.

3.6 Experimental

General Information. Unless otherwise stated, all reactions were performed under N_2 or vacuum using standard Schlenk techniques or in a N_2-filled drybox. All reaction temperatures for catalytic reactions refer to the temperature of pre-equilibrated oil or sand baths. All melting points were recorded on a Gallenkamp melting point apparatus and are uncorrected. ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra were recorded on a Bruker 500 MHz Avance spectrometer. Chemical shifts for ^{1}H and ^{13}C NMR are reported in ppm in reference to the residual ^{1}H and ^{13}C resonances of $CDCl_3$ (^{1}H: δ 7.24; ^{13}C: δ 77.23) and DMSO-d_6 (^{1}H: δ 2.50; ^{13}C: δ 39.51). Coupling constants are given in Hz. Elemental analyses were performed on a Perkin-Elmer 2400 CHN elemental analyzer. IR data were collected by Diffuse Reflectance Spectroscopy. $Pd(OAc)_2$ was purchased from PMO Pty Ltd, Australia. Aniline, *p*-methylaniline, *p*-acetoaniline, *p*-isopropylaniline, *p*-nitroaniline and phthalaldehyde were purchased from the Sigma-Aldrich Chemical Company and used as received. The syntheses of iminoisoindolines **1**, **2**, **4** and **5** have been reported in the literature,

however spectral data for these compounds have not been communicated and are thus included here.[23, 24]

General synthesis for iminoisoindolines 1-5.

Phthalaldehyde (17.2 mmol), aryl amine (36.1 mmol, 2.1 eq), formic acid (0.05 mL) and ether (30 mL) were combined in a 100 mL Schlenk flask equipped with a stir bar. The solution was stirred for 12 hours at ambient temperature under dinitrogen. The resulting precipitate was filtered and washed with ether (3x20 mL), then dried under vacuum to obtain white or yellow solids.

1-phenylimino-2-phenylisoindoline (1).

(75.0% yield, white powder, mp = 127.8 – 129.5ºC). ^{1}H NMR ($CDCl_3$, ppm) δ 8.01 (d, *J* = 6.0, 2H), 7.44 (d, *J* = 7.5, 1H), 7.38 (m, 3H), 7.31 (m, 2H), 7.04 (m, 3H), 6.99 (d, *J* = 6.7, 2H), 6.66 (d, *J* = 7.1, 1H), 4.94 (s, 2H); ^{13}C NMR ($CDCl_3$, ppm): δ 153.52, 150.87, 141.81, 140.59, 130.48, 129.34, 129.12, 127.53, 126.70, 123.33, 122.92, 122.44, 121.44, 120.18, 53.18. Anal. Calcd (%) for $C_{20}H_{16}N_2$: C 84.48, H 5.67, N 9.85; found: C 84.57, H 5.62, N 9.60.; FT-IR (KBr, cm^{-1})**:** 1646 (C=N), 1590, 1498. ESI-MS *m/z* calcd for $C_{20}H_{16}N_2$: 284.1313; found: 285.1392 $[M+H]^+$.

1-*p*-methylphenylimino-2-*p*-methylphenylisoindoline (2).

(51% yield, white powder). ^{1}H NMR ($CDCl_3$, ppm). δ 7.83 (d, *J* = 7.8, 2H), 7.41 (d, *J* = 7.6, 1H), 7.35 (m, 1H), 7.18 (d, *J* = 7.8, 2H), 7.11 (d, *J* = 7.4, 2H), 7.05 (m, 1H), 6.87 (d, *J* = 7.4, 2H), 6.71 (d, *J* = 7.6, 1H), 4.89 (s, 2H, CH_2), 2.36 (s, 3H, CH_3), 2.32 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$, ppm): δ 153.67, 148.37, 140.67, 139.29, 130.27, 129.89, 129.67, 129.38, 127.39, 126.70, 124.30, 122.87, 121.04, 121.44, 120.47, 53.27, 21.14, 21.03. Anal. Calcd (%) for $C_{22}H_{20}N_2$: C 84.58; H

6.45; N 8.97. Found: C 84.30; H 7.57; N 8.69. FT-IR (KBr, cm^{-1}): 1650 (C=N), 1633, 1615, 1615, 1609. ESI-MS *m/z* calcd for $C_{22}H_{20}N_2$: 312.1626; found: 313.1695 $[M+H]^+$.

1-*p*-isopropylphenylimino-2-*p*-isopropylphenylisoindoline (3).

(98% yield, white powder). ^1H NMR ($CDCl_3$): δ 7.88 (d, *J* = 7.9, 2H), 7.42 (d, *J* = 7.3, 1H), 7.35 (m, 1H), 7.24 (d, *J* = 7.5, 2H), 7.17 (d, *J* = 7.5, 2H), 7.05 (m, 1H), 6.91 (d, *J* = 7.5, 2H), 6.70 (d, *J* = 7.5, 1H), 4.91 (s, 2H, CH_2), 2.89 (m, 2H, CH(CH_3)$_2$), 1.28 (d, *J* = 6.7, 6H, CH(CH_3)$_2$), 1.25. (d, *J* = 6.7, 6H, CH(CH_3)$_2$). ^{13}C NMR ($CDCl_3$, ppm): δ 153.56, 148.58, 143.71, 143.00, 140.62, 139.56, 139.54, 131.81, 130.22, 127.38, 127.17, 126.96, 126.64, 122.85, 121.16, 120.20, 53.13, 33.74, 24.52, 24.25. Anal. Calcd (%) for $C_{24}H_{20}N_2O_2$: C 78.24; H 5.47; N 7.60. Found: C 78.45; H 5.17; N 7.38. FT-IR (KBr, cm^{-1}): 1648 (C=N), 1642, 1606. EI-MS *m/z* calcd for $C_{26}H_{28}N_2$: 368.2252; found: 368.2248.

1-*p*-acetophenylimino-2-*p*-acetophenylisoindoline (4).

Methanol was used in place of ether to obtain a higher yield (72% yield, yellow powder, mp: 170.5 -171.8 °C). ^1H NMR ($CDCl_3$, ppm): δ 8.10 (d, *J* = 8.4, 2H), 8.00 (d, *J* = 8.9, 2H), 7.99 (d, *J* = 8.4, 2H), 7.50 (d, *J* = 7.5, 1H), 7.43 (m, 1H), 7.09 (m, 1H), 7.04 (d, *J* = 8.4, 2H), 6.76 (d, J = 7.3, 1H), 5.00 (s, 2H, CH_2), 2.62 (s, 3H, CH_3), 2.58 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$, ppm): δ 197.3 (*C*OCH_3), 196.9 (*C*OCH_3), 154.8 (*C*=N), 152.7, 145.2, 140.0, 132.1, 131.9, 131.7, 131.2, 130.8, 130.2, 129.7, 126.3, 123.0, 120.8, 117.4, 99.9, 52.9, 25.5. Anal. Calcd (%) for $C_{24}H_{20}N_2O_2$: C 78.24; H 5.47; N 7.60. Found: C 78.45; H 5.17; N 7.38. FT-IR (KBr, cm^{-1}): 1662 (C=N), 1589. ESI-MS (*m/z*): calcd for $C_{24}H_{20}N_2O_2$: 368.1525; found: 369.1607 $[M+H]^+$.

1-*p*-nitrophenylimino-2-*p*-nitrophenylisoindoline (5).

(80% yield, yellow powder). ^{1}H NMR ($CDCl_3$): δ 8.27 (m, 4H), 8.17 (d, *J* = 9.3, 2H), 7.52 (m, 2H), 7.16 (m, 1H), 7.07 (d, *J* = 8.84, 2H), 6.78 (d, *J* = 7.90, 1H), 5.05 (s, 2H). ^{13}C NMR ($CDCl_3$): δ 156.4, 152.9, 146.6, 142.6, 142.0, 141.2, 132.1, 129.7, 128.0, 125.7, 125.5, 124.9, 124.0, 121.5, 119.4, 53.2. Anal. Calcd. for $C_{20}H_{14}N_4O_4$: C 64.48; H 3.77; N 14.97. Found: C 64.38; H 3.61; N 15.24.

General synthesis for palladacycles 6-9.

Iminoisoindoline (1.765 mmol) and $Pd(OAc)_2$ (1.765 mmol, 1.0 eq) were dissolved in dichloromethane (30 mL) in an oven dried 100 mL Schlenk flask equipped with a stir bar. After 12 h of stirring at ambient temperature under dinitrogen, the reaction mixture was filtered to remove palladium black. The filtrate was then concentrated and ether (30 mL) added to precipitate the desired palladacycle. The resulting precipitate was filtered, washed with cold ether (3x10 mL) then dried under vacuum. Crystals suitable for X-ray diffraction studies were obtained by slow evaporation from a 50:50 dichloromethane/hexane solution for **6** and **9**. Crystals of **7** were obtained from $CHCl_3$ and crystals of **8** were grown from a 50:50 acetone/hexane solution all at ambient temperature.

di(μ-acetato)-bis(1-phenylimino-2-phenylisoindoline)dipalladium(II) (6).

(42% yield, green powder, mp = 222.5 - 224.8ºC (decomp) ^{1}H NMR ($CDCl_3$, ppm) (**anti:syn = (*ca*) 3:1**); *anti-isomer* δ 7.67 (d, *J* = 7.6, 2H), 7.44-6.88 (m, 20H), 6.24 (d, *J* = 7.6, 2H), 5.68 (d, *J* = 8.1, 2H), 4.62 (d, *J* = 16.8, 2H), 3.61 (d, *J* = 16.8, 2H), 1.62 (s, 6H); *syn-isomer* 7.44-6.88 (m, 20H), 5.94 (m, 6H), 5.09 (s, 4H), 1.96 (s, 6H); ^{13}C NMR ($CDCl_3$, ppm): *anti-isomer* δ 179.33, 151.63, 146.37, 140.72, 136.67, 136.04, 131.01, 130.91, 129.01, 128.09, 127.67, 127.44, 127.21,

125.98, 125.90, 124.85, 124.56, 122.04, 121.97, 111.83, 52.93, 24.45. Anal. Calcd (%) for $C_{44}H_{36}N_4O_4Pd_2$: C 58.87, H 4.04, N 6.24; found: C 59.70, H 4.23, N 6.10; FT-IR (KBr, cm^{-1}) 1614 (C=N), 1603, 1585; EI-MS (*m/z*): calcd for $C_{44}H_{36}N_4O_4Pd_2$: 896.0806 [M], 897.0886 $[M+H]^+$; found 897.0878 $[M+H]^+$.

di(μ-acetato)-bis(1-*p*-methylphenylimino-2-*p*-methylphenylisoindoline)dipalladium(II) (7).

(46% yield, orange powder). ^1H NMR ($CDCl_3$): (**anti:syn = (*ca*) 3:1**); *anti-isomer* δ 7.47-6.96 (m, 12H), 6.85 (m, 4H) 6.57 (d, *J* = 7.9, 2H), 6.17 (d, *J* = 8.0, 2H), 5.74 (d, *J* = 8.0, 2H), 4.60 (d, *J* = 16.8, 2H), 3.77 (d, *J* = 16.8, 2H), 2.30 (s, 6H, -C*H*$_3$, aromatic), 2.20 (s, 6H, -C*H*$_3$, aromatic), 1.64 (s, 6H, acetate); *syn-isomer* δ 7.47-6.96 (m, 16H), (d, *J* = 7.9, 2H), 6.00 (d, *J* = 7.9, 4H), 5.04 (s, 4H), 2.42 (s, 6H, -C*H*$_3$, aromatic), 2.22 (s, 6H, -C*H*$_3$, aromatic), 1.98 (s, 6H, acetate); ^{13}C NMR ($CDCl_3$): *anti-isomer* δ 179.3, 151.1, 144.0, 140.7, 137.0, 135.4, 133.8, 131.1, 130.9, 130.7, 129.7, 127.9, 127.8, 127.4, 127.0, 125.9, 125.4, 124.1, 121.9, 111.4, 53.1, 24.6, 21.3, 20.9. Anal. calcd (%) for $C_{48}H_{45}N_4O_4Pd_2$: C 60.38; H 4.75; N 5.87. Found: C 60.43; H 4.64; N 6.95; FT-IR (KBr, cm^{-1}) 1619 (C=N), 1615, 1508. ESI-MS (*m/z*): calcd for $C_{48}H_{44}N_4O_4Pd_2$: 952.1432 [M], 893.1299 $[M-OAc]^+$; found 893.1554 $[M-OAc]^+$.

di(μ-acetato)-bis(1-*p*-isopropylphenylimino-*2*-*p*-isopropylphenylisoindoline)dipalladium(II) (8).

(30% yield, yellow powder). ^1H NMR ($CDCl_3$): (**anti:syn = (*ca*) 5:1**); *anti-isomer* δ 7.54 (s, 2H), 7.41 (m, 2H) 7.24 (d, *J* = 7.9, 2H), 7.00 (m, 4H), 6.83 (d, *J* = 7.9, 2H), 6.80 (d, *J* = 8.2, 2H), 6.65 (d, *J* = 8.2, 2H), 6.16 (d, *J* = 8.2, 2H), 5.83 (d, *J* = 8.2, 2H), 5.74 (d, *J* = 8.2, 2H), 4.53 (d, *J* = 16.9, 2H), 3.30 (d, *J* = 16.9, 2H), 2.91 (sept, *J* = 6.9, 2H, C*H*$(CH_3)_2$), 2.81 (sept, *J* = 6.9, 2H,

C*H*(CH_3)$_2$), 1.64 (s, 6H, acetate), 1.32 (d, *J* = 6.9, 6H, CH(C*H*$_3$)$_2$), 1.28 (d, *J* = 6.9, 6H, CH(C*H*$_3$)$_2$), 1.18 (d, *J* = 6.9, 12H, CH(C*H*$_3$)$_2$); *syn-isomer* δ 7.51 (d, *J* = 8.0, 2H), 7.34 (m, 4H), 7.31 (d, *J* = 7.9, 2H), 7.24 (m, 4H), 7.20 (d, *J* = 7.9, 2H), 7.00 (m, 2H), 7.10 (d, *J* = 7.9, 2H), 6.90 (d, *J* = 7.9, 2H), 5.83 (m, 2H), 5.05 (s, 4H), 2.98 (m, 4H), 1.98 (s, 6H, acetate), 1.30 (d, *J* = 6.9, 6H, CH(C*H*$_3$)$_2$), 1.25 (d, *J* = 6.9, 6H, CH(C*H*$_3$)$_2$), 1.20 (d, *J* = 6.9, 12H, CH(C*H*$_3$)$_2$); ^{13}C NMR ($CDCl_3$): *anti-isomer* δ 179.0, 151.5, 146.5, 144.2, 142.3, 140.9, 134.4, 134.3, 131.1, 130.7, 128.0, 127.5, 127.3, 126.8, 125.7, 125.2, 124.9, 122.9, 122.0, 111.6, 52.8, 34.0, 33.8, 24.59, 24.57, 24.5, 24.3, 24.1. Anal. calcd (%) for $C_{56}H_{62}N_4O_4Pd_2$: C 63.10; H 5.67; N 5.26. Found: C 62.96; H 5.68; N 5.32; FT-IR (KBr, cm^{-1}): 1615.4 (C=N), 1578.9, 1552.1, 1504.2, 1415.1; ESI-MS (*m/z*): calcd for $C_{56}H_{60}N_4O_4Pd_2$: 1067.2841 [M], 1005.2551 [M-OAc]$^+$; found 1005.2647 [M-OAc]$^+$.

di(μ-acetato)-bis(1-*p*-acetophenylimino-2-*p*-acetophenylisoindoline)dipalladium(II) (9).

(40% yield, orange powder, mp = 242.5 – 244.5°C (decomp.)). ^{1}H NMR ($CDCl_3$, ppm): (**anti:syn = (*ca*) 8:1**); *anti-isomer:* δ 8.26 (s, 2H), 7.85 (d, *J* = 8.0, 2H), 7.53 (m, 4H), 7.38 (m, 4H), 7.10 (d, *J* = 8.2, 2H), 7.04 (m, 2H), 6.36 (d, *J* = 8.5, 2H), 5.95 (d, *J* = 8.0, 2H), 5.77 (d, *J* = 8.1, 2H), 4.76 (d, *J* = 16.8, 2H), 3.82 (d, *J* = 16.8, 2H), 2.58 (s, 6H, $COCH_3$), 2.56 (s, 6H, $COCH_3$), 1.66 (s, 6H, OAc): *syn-isomer;* 8.10 (d, *J* = 7.9, 4H), 7.90 (m, 6H), 7.56-7.02 (m, 8H), 5.95 (d, *J* = 7.9, 4H), 5.17 (s, 4H, C*H*$_2$), 2.67 (s, 6H, COC*H*$_3$), 2.65 (s, 6H, COC*H*$_3$), 1.96 (s, 6H, OAc); ^{13}C NMR (DMSO, ppm): *anti-isomer* δ 197.07, 196.64, 178.60, 151.37, 150.01, 141.42, 138.73, 135.66, 134.47, 131.92, 130.13, 129.90, 128.97, 127.76, 126.94, 126.59, 126.11, 125.26, 123.18, 122.71, 112.79, 53.49, 26.68, 26.23, 24.41, 21.03. Anal. Calcd (%) for $C_{52}H_{44}N_4O_4Pd_2$: C 58.60, H 4.16, N 5.26; found: C 58.38, H 4.01, N 5.13; FT-IR (KBr, cm^{-1})**:** 1667 (C=N), 1623, 1484; ESI-MS (*m/z*): calcd for $C_{52}H_{44}N_4O_8Pd_2$: 1064.1229 [M], 1005.1096 [M-OAc]$^+$; found 1005.2597 [M-OAc]$^+$.

General procedure for Heck coupling reactions

In a typical run, an oven-dried 25 mL two-necked flask equipped with a stir bar was charged with a known mol % catalyst and base (2.0 mmol). Under nitrogen, DMA (3 mL), aryl halide (1.0 mmol) and n-butylacrylate (2.0 mmol) were added via syringe. The flask was then placed in a pre-heated sand bath at 145 ^{o}C. After the specified time the flask was removed from the sand bath and water (20 mL) was added followed by extraction with dichloromethane (4x10 mL). The combined organic layers were washed with water (3x10 mL), dried over anhydrous $MgSO_4$, and filtered. Solvent was removed under vacuum. The residue was dissolved in $CDCl_3$ and analyzed by ^{1}H NMR. Percent conversions were determined against the remaining aryl halide.[40-43]

General procedure for Suzuki coupling reactions

In a typical run, an oven dried 25 mL two-necked flask equipped with a stir bar was charged with a known mol % catalyst, base (2.0 mmol) and phenylboronic acid (1.5 mmol). Under nitrogen, DMA (3 mL) and aryl halide (1.0 mmol) were added via syringe. The flask was placed in pre-heated sand bath at 80 ^{o}C. After the specified time the flask was removed from the sand bath and water (20 mL) was added followed by extraction with dichloromethane (3x10 mL). The combined organic layers were washed with water (3x10 mL), dried over anhydrous $MgSO_4$, and filtered. Solvent was removed under vacuum. The residue was dissolved in $CDCl_3$ and analyzed by ^{1}H NMR. Percent conversions were determined against the remaining aryl halide. [40-43]

X-ray structure determinations

Data were collected at -100 ºC on a Nonius Kappa CCD diffractometer, using the COLLECT program.[44] Cell refinement and data reductions used the programs DENZO and

SCALEPACK.[45] SIR97[46] was used to solve the structures and SHELXL97[47] was used to refine the structures. ORTEP-3 for Windows[48] was used for molecular graphics and PLATON[49] was used to prepare material for publication. H atoms were placed in calculated positions with U_{iso} constrained to be 1.5 times U_{eq} of the carrier atom for methyl protons and 1.2 times U_{eq} of the carrier atom for all other hydrogen atoms. For complex **9**, there are four acetyl groups in the molecule, attached on atoms C12, C18, C42 and C48. The acetyl group on C48 is badly disordered and would not refine to reasonable bond angles and bond lengths. To avoid putting meaningless values into the CSD, the average of the bond lengths and bond angles of the other three acetyl groups was used to form a rigid acetyl group on C48. The thermal ellipsoids on C52 and O51 were restrained using the ISOR command in SHELXL. The resulting displacements for these atoms were much larger than for the equivalent groups. Consequently, C52 (and the attached H atoms) and O51 had very large U_{eq}.

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Supporting Information Available: Full crystallographic data for compounds **6·CH_2Cl_2, 7·$CHCl_3$, 8·Acetone** and **9·CH_2Cl_2** are available as CIF files.

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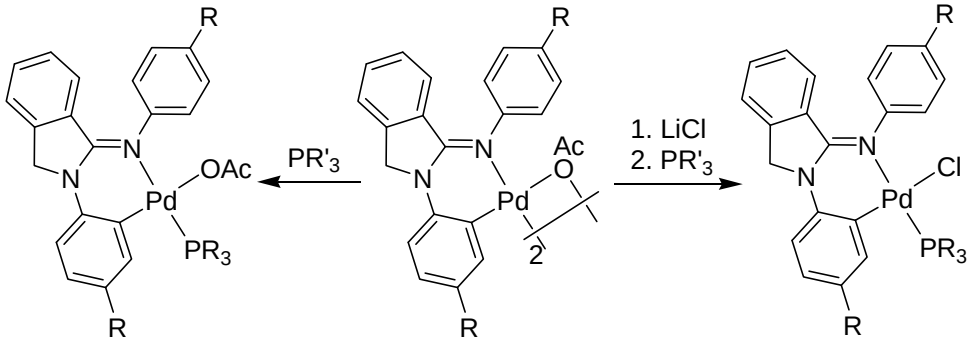
CHAPTER 4

PUBLICATION 3

Description

The following is a verbatim copy of an article published in January of 2009 in the Journal of Organometallic Chemistry (*J. Organomet. Chem.,* **2009**, *694*, 1542-1548) and describes the synthesis and characterization of a series of six-membered iminoisoindoline-based mononuclear palladacycles of the general formula [Pd(iminoisoindoline)(X)PR_3], R = Cy, Ph; X = Cl, OAc, which were prepared in a three-step protocol from commercially available starting materials. All compounds (**5-14**) were synthesized and characterized by standard methods, and their molecular structures determined by single crystal X-ray analysis



Authors' Contribution

I synthesized and fully characterized all phosphine-ligated mononuclear iminoisoindoline-based palladacycles (**5-14**). Dr. J. Wilson Quail did all the structure determination by single crystal X-ray analysis and the work was supervised by Dr. Stephen R. Foley.

Relation of Chapter 4 (Publication 3) to the overall Objectives of this Project

In the literature, mononuclear palladacycles were found to be more active than their dinuclear counterparts. This chapter, therefore, looks at the reaction of phosphines (PR_3, R = Ph, Cy) with the dinuclear iminoisoindoline-based palladacycles (Chapter 3), yielding phosphine-ligated mononuclear palladacycles. This was done so that their activities in the C-C coupling reactions could be compared with their corresponding dinuclear acetate-bridged complexes.

4. Mononuclear Palladacycles of *N*,*N*'-Diaryl-2-iminoisoindolines

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4.1 Abstract

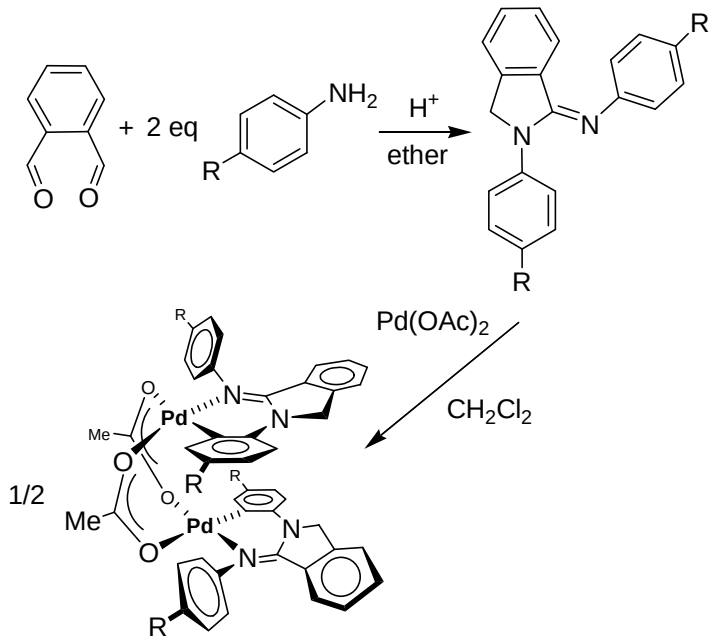
Reaction of acetato-bridged dinuclear palladacycles, [Pd(iminoisoindoline)(μ-OAc)]$_2$, with equimolar amounts of PR_3 (where R = Ph or Cy) resulted in formation of the corresponding mononuclear phosphine-ligated, six-membered palladacycles with the general formula [Pd(iminoisoindoline)(OAc)PR_3]. The analogous chloride complexes were synthesized by reaction of [Pd(iminoisoindoline)(μ-OAc)]$_2$ with LiCl in acetone followed by addition of phosphine to afford the monomeric derivatives [Pd(iminoisoindoline)(Cl)PR_3]. Representative crystal structures of both types of mononuclear palladacycles confirmed the mononuclear nature of the complexes and showed a trans-arrangement of the phosphine ligand to the heterocyclic imine-nitrogen of the palladacycles.

4.2 Introduction

Isoindoline derivatives have found widespread applications in the pharmaceutical, herbicidal and dye industries. For example pazinaclone, staurosporine, and indoprofen all possess an isoindoline substructure.[1] We are interested in one particular family of isoindolines,

specifically *N,N'*-diaryl-2-iminoisoindolines for applications as ligands in group 10 coordination chemistry. The specific interest in diarylliminoisoindolines lies in their extreme ease of synthesis, the ease in which they can be sterically and electronically tuned and their potential ability to form metallacycles. Despite their ease of synthesis, iminoisoindolines remain relatively unexplored as ligands. While the original synthesis for diphenyliminoisoindoline dates back to 1910,[2] few reports exist concerning *N,N'*-diaryl-2-iminoisoindolines indicating few applications have been found for this isoindoline subclass.[1,3,4] *N,N'*-Diaryl-2-iminoisoindolines are easily synthesized by reaction of phthalaldehyde with two equivalents of an aryl amine in ether as solvent (Scheme 1). The resulting iminoisoindoline usually precipitates from solution as an analytically pure solid, allowing for easy isolation.[1, 5]

We have recently shown that the reaction proceeds through a double condensation reaction to form a γ-diimine which then undergoes intramolecular cyclization to form the corresponding iminoisoindoline.[6] *para*-Substituted *N,N'*-diaryl-2-iminoisoindolines readily react with $Pd(OAc)_2$ at room temperature resulting in formation of six-membered [C,N] dinuclear cyclopalladated complexes with the general formula $[Pd(iminoisoindoline)(\mu\text{-}OAc)]_2$ (Scheme 4.1).[5]



Scheme 4.1. Synthesis of iminoisoindoline ligands and corresponding acetato-bridged dinuclear palladacycles

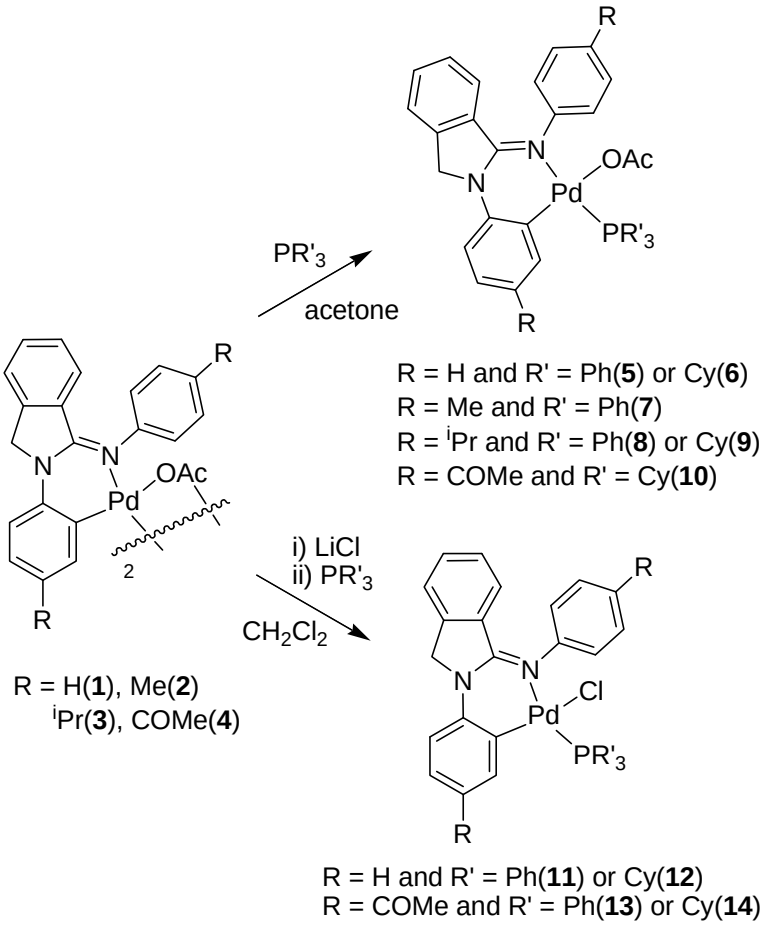
Palladacycles represent an increasingly important class of organometallic compounds, where their influence is especially dominant in the field of coupling reactions for organic transformations.[7-16] Many palladium-mediated coupling reactions are thought to involve palladacyclic intermediates[17-19] and several palladacycles are also reported to be biologically active compounds for cancer therapy.[20, 21] Herein we report the synthesis and characterization of mononuclear iminoisoindoline-based six-membered palladacycles with the general formula [Pd(iminoisoindoline)(OAc)(PR_3)] and [Pd(iminoisoindoline)(Cl)PR_3].

4.3 Results and Discussion

4.3.1 Synthesis and characterization of [Pd(iminoisoindoline)(OAc)(PR_3)] complexes

We previously described the formation of six-membered, acetato-bridged dinuclear palladacycles (**1-4**) of the general formula [Pd(iminoisoindoline)(μ-OAc)]$_2$ from the reaction of the corresponding iminoisoindoline with $Pd(OAc)_2$.[5] The solid state structures of these complexes show that they adopt a characteristic closed book conformation where the two iminoisoindoline ligands are stacked on top of each other in an *anti* configuration. In an extension of our previously reported work, we describe here the synthesis and characterization of a series of mononuclear phosphine-ligated, six-membered palladacycles from complexes **1-4**.

Palladacycles **5-10**, of the general formula [Pd(iminoisoindoline)(OAc)(PR_3)], (where R = Ph or Cy), were obtained by the reaction of acetato-bridged dinuclear palladacycles (**1-4**) with stoichiometric amounts of phosphine in acetone at room temperature (Scheme 4.2). Thus, treatment of dinuclear complexes **1-3** with two equivalents of PPh_3 afforded the corresponding mononuclear phosphine-ligated complexes **5**, **7** and **8** in good yield as yellow solids. Analogous treatment of complexes **1**, **3** and **4** with PCy_3 also afforded the corresponding mononuclear tricyclohexylphosphine-ligated complexes **6**, **9** and **10** (Scheme 4.2).



Scheme 4.2. Synthesis of mononuclear iminoisoindoline-based palladacycles

The mononuclear palladacycles were obtained in good to excellent yields (60-94%) and were fully characterized by elemental analysis, mass spectrometry and NMR spectroscopy. A characteristic indication of the formation of mononuclear species is the observed ^{1}H NMR resonance for the CH_2 protons of the iminoisoindoline ring. In dinuclear complexes **1**-**4**, the methylene protons are diastereotopic resulting in formation of two doublets each integrating for one proton at ~4.6 and ~3.5 ppm. After reaction with phosphine, the ^{1}H NMR spectra show the disappearance of the two doublets coincident with the appearance of a new singlet at ~5 ppm integrating for two protons indicating the methylene protons are now chemically equivalent and

the new complexes have an average C_s symmetry in solution. The free iminoisoindoline ligands also show a singlet which is ~0.1 ppm upfield relative to that of phosphine-ligated palladacycles.[5, 6] The ^{31}P NMR spectra of these complexes show a singlet at ~33 ppm consistent with only one isomer being present in solution. The mass spectra of all complexes show a strong signal which was assigned to their respective molecular cation $[M\text{-}OAc]^+$.

4.3.2 Synthesis and Characterization of [Pd(iminoisoindoline)(Cl)(PR_3)] Complexes

The acetato-bridged dinuclear palladacycles **1** and **4** were treated with LiCl in acetone at room temperature resulting in formation of a yellow precipitate which was presumably the chloride-bridged analogue of **1** and **4**. The products were not characterized but used as is for the subsequent steps. Addition of LiCl is a general route for the conversion of acetate-bridged dinucler palladacycles to their chloro-bridged analogues.[7-12] The resulting yellow powder was isolated and suspended in dichloromethane. Palladacycles **11-14**, of the general formula [Pd(iminoisoindoline)(Cl)PR_3], (where R = Ph or Cy), were obtained by the reaction of the yellow suspension with stoichiometric amounts of phosphine at room temperature (Scheme 4.2). Over the course of 12 h, the yellow suspension gradually became a clear solution which, after work up, afforded the desired products. Thus, treatment of dinuclear complexes **1** and **4** with LiCl followed by two equivalents of PPh_3 afforded the corresponding mononuclear phosphine-ligated complexes **11** and **13** in good yields (84 and 78%, respectively). Analogous treatment of complexes **1** and **4** with LiCl and PCy_3 also afforded the corresponding mononuclear tricyclohexylphosphine-ligated complexes **12** and **14** in 80 and 90% yields, respectively (Scheme 4.2). The NMR spectra were consistent with those observed for the mononuclear acetato analogues **5-10**. The mass spectra of

all complexes show a strong signal which was assigned to their respective molecular cation $[M-Cl]^+$.

4.3.3 Crystal structures of complexes 5, 10, 12 and 13.

To further clarify the coordination environment around the metal center, representative molecular structures of **5-14** have been ascertained by means of X-ray diffraction studies. Single crystals of complexes **5**, **10**, **12** and **13** were obtained by slow evaporation of a concentrated dichloromethane/hexane (1:1) solution. ORTEP plots are shown in Figures 4.1-4.4, and included in their respective captions are selected bond distances and angles. Palladacycle **10** and **15** co-crystallized with a molecule of dichloromethane. Table 4.1 shows selected crystal data and refinement parameters for the structures. In all four palladacyclic compounds, the crystal structures revealed mononuclear species with a slightly distorted square-planar coordination geometry around the palladium atom. The environment around each palladium atom consists of a bidentate iminoisoindoline [C,N], a terminal chloride or acetate and a phosphine. Consistent with other reports of mononuclear palladacycles, the phosphine ligands are always *trans* to the donor N atom of the iminoisoindoline ligand.[22-24] In all four palladacycles the Pd-P bond distances range from 2.274 to 2.290 Å. The Pd-$C_{palladate}$ bond distances are all similar at 2.00(1) Å, consistent with published reports.[22-24]

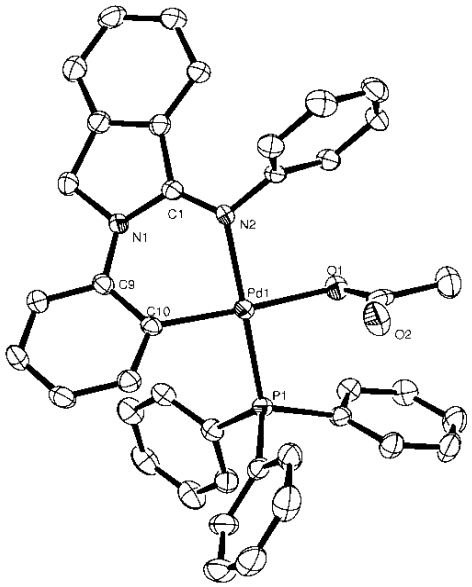


Figure 4.1. ORTEP plot of **5** at the 50% probability level. The hydrogen atoms have been omitted for clarity. Selected bond lengths [Å] and angles [^{0}]: Pd(1)-C(10) = 1.998(3), Pd(1)-N(2) = 2.086(2), Pd(1)-O(1) = 2.092(2), Pd(1)-P(1) = 2.2739(8), C(10)-Pd(1)-N(2) = 87.23(10), C(10)-Pd(1)-O(1) = 174.97(10), N(2)-Pd(1)-O(1) = 90.55(9), C(10)-Pd(1)-P(1) = 93.83(8), N(2)-Pd(1)-P(1) = 171.92(7), O(1)-Pd(1)-P(1) = 87.74(6).

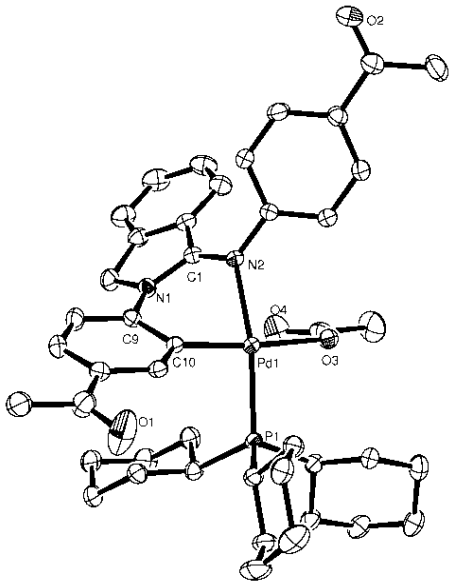


Figure 4.2. ORTEP plot of **10** at the 30% probability level. The hydrogen atoms have been omitted for clarity. Selected bond lengths [Å] and angles [^{o}]: Pd(1)-C(10) = 1.987(3), Pd(1)-N(2) = 2.138(2), Pd(1)-O(3) = 2.1142(19), Pd(1)-P(1) = 2.2767(7), C(10)-Pd(1)-N(2) = 83.42(9), C(10)-Pd(1)-O(3) = 174.58(9), N(2)-Pd(1)-O(3) = 91.30(8), C(10)-Pd(1)-P(1) = 91.80(7), N(2)-Pd(1)-P(1) = 167.71(6), O(3)-Pd(1)-P(1) = 93.15(5).

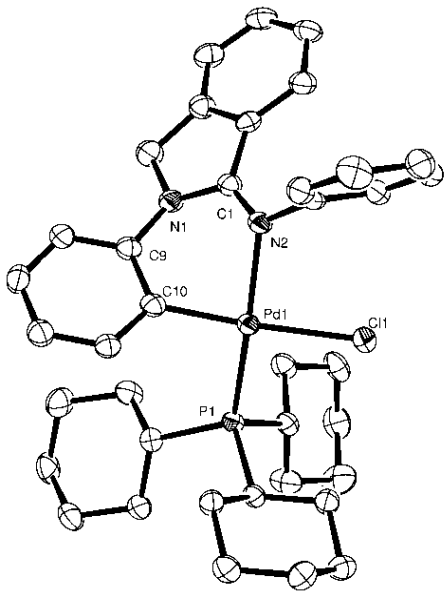


Figure 4.3. ORTEP plot of **12** at the 50% probability level. The hydrogen atoms have been omitted for clarity. Selected bond lengths [Å] and angles [^{o}]: Pd(1)-C(10) = 1.995(3), Pd(1)-N(2) = 2.130(3), Pd(1)-Cl(1) = 2.4077(9), Pd(1)-P(1) = 2.2901(8), C(10)-Pd(1)-N(2) = 84.26(12), C(10)-Pd(1)-Cl(1) = 174.30(9), N(2)-Pd(1)-Cl(1) = 91.17(8), C(10)-Pd(1)-P(1) = 94.38(9), N(2)-Pd(1)-P(1) = 166.64(8), Cl(1)-Pd(1)-P(1) = 90.85(3).

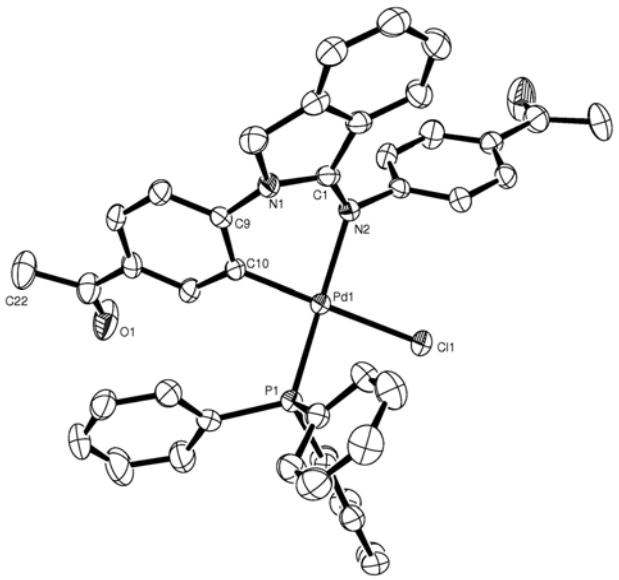


Figure 4.4. ORTEP plot of **13** at the 50% probability level. The hydrogen atoms have been omitted for clarity. Selected bond lengths [Å] and angles [^{0}]: Pd(1)-C(10) = 1.992(4), Pd(1)-N(2) = 2.110(3), Pd(1)-Cl(1) = 2.3990(10), Pd(1)-P(1) = 2.2540(11), C(10)-Pd(1)-N(2) = 85.25(14), C(10)-Pd(1)-Cl(1) = 174.02(11), N(2)-Pd(1)-Cl(1) = 94.47(9), C(10)-Pd(1)-P(1) = 93.93(11), N(2)-Pd(1)-P(1) = 160.16(9), Cl(1)-Pd(1)-P(1) = 88.35(4).

Table 4.1. Crystal data and refinement parameters for complexes **5**, **10·CH_2Cl_2**, **12** and **13·CH_2Cl_2**

	5	**10·CH_2Cl_2**	**12**	**13·CH_2Cl_2**
formula	$C_{40}H_{33}N_2O_2PPd$	$C_{45}H_{57}Cl_2N_2O_4PPd$	$C_{38}H_{48}ClN_2PPd$	$C_{43}H_{36}Cl_3N_2O_2PPd$
fw	711.05	898.20	705.60	856.46
Color	Pale yellow	yellow	yellow	yellow
Crystal size, mm^3	0.22 x 0.12 x 0.12	0.18 x 0.11 x 0.08	0.25 x 0.20 x 0.18	0.15 x 0.15 x 0.10
Crystal system	Triclinic	Triclinic	Monoclinic	Monoclinic
Space group	P-1	P-1	P21/c	P21/c
a, Å	10.2458(3)	9.8823(2)	11.7619(2)	17.0313(4)
b, Å	12.6323(3)	12.1332(2)	19.3702(4)	15.4993(3)
c, Å	13.8280(3)	17.9651(3)	15.9664(3)	29.3952(8)
α, deg	83.401(2)	88.5070(10)	90	90
β, deg	81.0430(10)	86.9870(10)	113.0660(10)	90.6215(9)
γ, deg	66.857(2)	81.5910(10)	90	90
Z	2	2	4	4
ρ_{calc}, Mg m^{-3}	1.455	1.402	1.400	1.466
T, K	173(2)	173(2)	173(2)	173(2)
Collec./Ind. Ref.	23729/7437	49446/14683	44459/6834	60310/8877
R(int)	0.0563	0.0731	0.0850	0.0997
F(000)	728	936	1472	3488
θ range, deg	3.28 to 27.53	2.06 to 31.99	2.52 to 26.37	1.78 to27.48
FinalR_1(I >2σI)	R1 = 0.0411,	R1 = 0.0555,	R1 = 0.0427,	R1 = 0.0529
	wR2 = 0.0810	wR2 = 0.1099	wR2 = 0.0955	wR2 = 0.1046
R_1(all data)	R1 = 0.0550,	R1 = 0.0903,	R1 = 0.0595,	R1 = 0.0970
	wR2 = 0.0884	wR2 = 0.1259	wR2 = 0.1064	wR2 = 0.1216

4.4 Conclusion

We have successfully synthesized and characterized a series of six-membered, mononuclear iminoisoindoline-based palladacycles as air and moisture stable complexes. Much of the recent activity in palladacyclic chemistry has been prompted by the fact that they are particularly good precatalysts for carbon-carbon bond forming reactions. Mononuclear trialkylphosphine-ligated palladacycles have been shown to be especially effective for Suzuki and Heck coupling chemistry.[23, 25] Currently in progress are catalytic studies of these mononuclear complexes in C-C coupling reactions and this work will be reported at a later date.

4.5 Experimental

General

Unless otherwise stated, all reactions were performed under N_2 using standard Schlenk techniques or in a N_2-filled drybox. Solvents were dried using a MBraun solvent purification system and stored under nitrogen. ^{1}H, ^{31}P and ^{13}C $\{^{1}H\}$ NMR spectra were recorded on a Bruker 500 MHz Avance spectrometer. Chemical shifts for ^{1}H and ^{13}C NMR are reported in ppm in reference to the residual ^{1}H and ^{13}C resonances of $CDCl_3$ (^{1}H: δ 7.24; ^{13}C: δ 77.23). ^{31}P NMR chemical shifts are also reported in ppm with respect to 85% H_3PO_4, set to zero as an external standard. Coupling constants are given in Hz. High resolution mass spectra (HRMS) were measured on an Applied Biosystem QSTAR® XL MS/MS system (ESI-QTOF). Elemental analyses were performed on a Perkin-Elmer 2400 CHN elemental analyzer. $[Pd(iminoisoindoline)(\mu\text{-}OAc)]_2$ complexes were synthesized following literature procedures.[5] Tricyclohexylphosphine, triphenylphosphine, aniline, *p*-acetoaniline, *p*-isopropylaniline, *p*-

tertiarybutylaniline were purchased from the Sigma-Aldrich Chemical Company. Phthalaldehyde was purchased from Alfa Aesar. All chemicals were used as received.

General procedure (A) for synthesis of [Pd(iminoisoindoline)(OAc)(PR_3)] complexes 5-10.

A flask was charged with [Pd(iminoisoindoline)(μ-OAc)]$_2$, (**1**-**4**) and either triphenylphosphine or tricyclohexylphosphine (stoichiometric amounts) in acetone (30 mL, degassed). The resulting suspension slowly became a clear, colourless solution over the course of 12 h. The resulting solution was filtered and the filtrate was concentrated to circa 2 mL. Hexanes were then added to precipitate out the desired complex, which was filtered, washed with 3x10 mL of hexanes, and then dried under vacuum. Single crystals of palladacycles **5** and **10** were obtained from slow evaporation of a dichloromethane/hexane (1:1) solution.

Synthesis of [Pd(*N,N'*-diphenyl-2-iminoisoindoline)(OAc)PPh_3] (5)

Compound **5** was obtained as a yellow powder in 94% yield from palladacycle **1 (**203 mg, 0.226 mmol) and triphenylphosphine (130 mg, 0.497 mmol) using procedure A. ^{1}H NMR ($CDCl_3$, ppm) δ 7.51 (m, 7H, Ar), 7.39 (m, 1H, Ar), 7.33 (m, 3H, Ar), 7.27 (m, 10H, Ar), 7.22 (m, 1H, Ar), 7.00 (m, 2H, Ar), 6.87 (m, 1H, Ar), 6.75 (m, 1H, Ar), 6.23 (m, 1H, Ar), 6.03 (d, *J* = 8.0, 1H, Ar), 5.16 (s, 2H, -C*H*$_2$-), 1.04 (s, 3H, CO_2C*H*$_3$); ^{13}C NMR ($CDCl_3$, ppm): δ 175.36 (*C*O_2CH_3), 155.94 (*C*=N), 146.27, 141.24, 140.21, 140.10, 137.68, 134.71, 134.62, 131.65, 131.58, 130.89, 130.82, 130.44, 130.15, 129.61, 128.78, 128.24, 128.15, 127.92, 127.60, 127.52, 127.33, 126.30, 125.30, 124.05, 122.66, 122.19, 124.33, 51.63 (-*C*H$_2$-), 23.69 (CO_2*C*H$_3$). ^{31}P NMR ($CDCl_3$, ppm) δ 34.04. Elemental analysis (%) calcd for $C_{40}H_{33}N_2O_2PPd\cdot(CH_2Cl_2)_{0.7}$: C 63.44, H 4.50, N 3.64; found: C 63.17, H 4.40, N 3.96 (^{1}H NMR analysis of sample showed presence of 0.6 equiv of

CH_2Cl_2 which was used as the crystallization solvent). HRMS *m/z* calcd. for $C_{40}H_{33}N_2O_2PPd$: 710.1314 [M], 651.1181 $[M\text{-}OAc]^+$ found 651.1155 $[M\text{-}OAc]^+$.

Synthesis of [Pd(N,N'-diphenyl-2-iminoisoindoline)(OAc)PCy_3] (6)

Compound **6** was obtained as a yellow powder in 90% yield from palladacycle **1** (341 mg, 0.380 mmol) and tricyclohexylphosphine (224 mg, 0.799 mmol) using procedure A. ^1H NMR ($CDCl_3$, ppm) δ 7.47 (m, 2H, Ar), 7.39 (m, 1H, Ar), 7.26 (m, 2H, Ar), 7.18 (m, 3H, Ar), 7.00 (m, 2H, Ar), 6.84 (m, 2H, Ar), 6.15 (d, *J* = 8.1, 1H, Ar), 5.08 (s, 2H, -C*H*$_2$-), 2.01 (m, 3H, PCy_3), 1.82 (m, 6H, PCy_3), 1.71 (m, 6H, PCy_3), 1.63 (m, 3H, PCy_3), 1.59 (s, 3H, CO_2CH_3), 1.42(m, 6H, PCy_3), 1.13(m, 9H, PCy_3); ^{13}C NMR ($CDCl_3$, ppm): δ 176.43 CO_2CH_3), 157.18 (C=N), 146.63, 141.98, 140.63, 140.56, 139.54, 134.28, 131.16, 130.75, 128.52, 127.17, 126.48, 126.48, 125.36, 124.08, 123.38, 123.35, 122.63, 114.26, 51.49 (-*C*H$_2$-), 33.28, 33.11, 29.72, 28.14, 28.05, 26.76, 25.71. ^{31}P NMR ($CDCl_3$, ppm) δ 32.96. Elemental analysis (%) calcd for $C_{40}H_{51}N_2O_2PPd$: C 65.88, H 7.05, N 3.39.; found: C 65.58, H 7.04, N 3.64. HRMS *m/z* calcd. for $C_{40}H_{51}N_2O_2PPd$: 728.2723 [M], 669.2590 $[M\text{-}OAc]^+$ found 669.2574 $[M\text{-}OAc]^+$.

[Pd(*N,N'*-di(p-methylphenyl)-2-iminoisoindoline)(OAc)PPh_3] (7)

Compound **7** was obtained as a yellow powder in 70% yield from palladacycle **2** (237 mg, 0.249 mmol) and triphenylphosphine (144 mg, 0.549 mmol) using procedure A. ^1H NMR ($CDCl_3$, ppm) δ 7.49 (m, 8H, Ar), 7.35 (m, 5H, Ar), 7.27 (m, 4H, Ar), 7.13 (d, *J* = 7.4, 2H, Ar), 7.02 (m, 3H, Ar), 6.82 (d, *J* = 7.8, 1H, Ar), 6.66 (d, *J* = 7.0, 1H, Ar), 6.47 (br, s, 1H, Ar), 6.14 (d, *J* = 7.8, 1H, Ar), 5.12 (s, 2H, -C*H*$_2$-), 2.32 (s, 3H, C_6H_4-C*H*$_3$), 1.57 (s, 3H, C_6H_3-C*H*$_3$), 1.07 (s, 3H, CO_2CH_3); ^{13}C NMR ($CDCl_3$, ppm): δ 176.06 (CO_2CH_3), 156.17 (C=N), 144.24, 141.65, 136.23, 135.38, 135.29, 135.18, 132.29, 131.64, 131.28, 131.12, 131.07, 129.51, 129.10, 128.65, 128.11,

128.02, 127.82, 127.11, 126.58, 126.12, 125.51, 124.99, 122.45, 114.01, 52.08 (-*C*H_2-), 24.30 (C_6H_4-*C*H_3), 21.35 (C_6H_3-*C*H_3), 20.21 CO_2*C*H_3). ^{31}P NMR ($CDCl_3$, ppm) δ 33.90. Elemental analysis (%) calcd. for $C_{42}H_{37}N_2O_2PPd$: C 68.25, H 5.05, N 3.79; found: C 67.89, H 4.97, N 3.84. HRMS m/z calcd. for $C_{42}H_{37}N_2O_2PPd$: 738.1627 [M], 679.1494 $[M\text{-}OAc]^+$ found 679.1475 $[M\text{-}OAc]^+$.

[Pd(N,N'-di(p-isopropylphenyl)-2-iminoisoindoline)(OAc)PPh_3] (8)

Compound **8** was obtained as a yellow powder in 60% yield from palladacycle **3** (255 mg, 0.239 mmol) and triphenylphosphine (144 mg, 0.549 mmol) using procedure A. ^{1}H NMR ($CDCl_3$, ppm) δ 7.52 (m, 6H, Ar), 7.45 (d, *J* = 7.6, 1H, Ar), 7.35 (m, 5H, Ar), 7.25 (m, 5H, Ar), 7.18 (d, *J* = 8.2, 2H, Ar), 7.09 (d, *J* = 8.2, 2H, Ar), 6.96 (m, 1H, Ar), 6.92 (d, *J* = 8.4, 1H, Ar), 6.77 (m, 2H, Ar), 5.99 (d, *J* = 8.2, 1H, Ar), 5.13 (s, 2H, -C*H*$_2$-), 2.88 (sept, *J* = 6.9, 1H, -C*H*$(CH_3)_2$), 2.10 (sept., *J* = 6.9, 1H, -C*H*$(CH_3)_2$), 1.22 (d, *J* = 6.9, 6H, -CH(C*H*$_3)_2$), 1.05 (s, 3H, CO_2C*H*$_3$), 0.61 (d, *J* = 6.9, 6H, -CH(C*H*$_3)_2$); ^{13}C NMR ($CDCl_3$, ppm): δ 176.01 (-*C*O_2CH_3), 155.82 (*C*=N), 146.25, 144.55, 143.03, 141.53, 136.41, 135.53, 135.44, 135.36, 131.87, 131.50, 131.13, 131.01, 130.03, 128.65, 128.40, 128.12, 128.04, 127.76, 127.14, 126.74, 126.30, 122.61, 122.37, 114.45, 52.32 (-*C*H_2-), 33.91 (-*C*$H(CH_3)_2$), 33.11 (-*C*$H(CH_3)_2$), 24.33 (-CH(*C*$H_3)_2$), 23.98 (-CO_2*C*H_3), 23.54 (-CH(*C*$H_3)_2$). ^{31}P NMR ($CDCl_3$, ppm) δ 34.20. Elemental analysis (%) calcd. for $C_{46}H_{45}N_2O_2PPd$: C 69.47, H 5.70, N 3.52; found: C 69.30, H 5.48, N 3.70. HRMS *m/z* calcd. for $C_{46}H_{45}N_2O_2PPd$: 794.2253 [M], 735.2120 $[M\text{-}OAc]^+$ found 735.2088 $[M\text{-}OAc]^+$.

[Pd(N,N'-di(p-isopropylphenyl)-2-iminoisoindoline)(OAc)PCy_3] (9)

Compound **9** was obtained as a yellow powder in 82% yield from palladacycle **3** (250 mg, 0.235 mmol) and tricyclohexylphosphine (139 mg, 0.496 mmol) using procedure A. ^{1}H NMR

($CDCl_3$, ppm) δ 7.44 (d, *J* = 7.5, 1H, Ar), 7.36 (m, 2H, Ar), 7.09 (d, *J* = 8.3, 2H, Ar), 7.05 (d, *J* = 8.3, 2H, Ar) 6.98 (m, 1H, Ar), 6.83 (d, *J* = 8.2, Ar), 6.77 (d, *J* = 8.2, 1H, Ar), 6.14 (d, *J* = 8.1, 1H, Ar), 5.03 (s, 2H, -C*H*$_2$-), 2.91 (sept., *J* = 6.9, 1H, -CH(CH_3)$_2$), 2.77 (sept., *J* = 6.9, 1H, -C*H*(CH_3)$_2$), 2.01 (m, 3H, PCy_3), 1.84 (m, 7H, PCy_3), 1.69 (m, 7H, PCy_3), 1.61 (m, 4H, PCy_3), 1.57 (s, 3H, -CO_2C*H*$_3$), 1.38 (m, 6H, PCy_3), 1.22 (m, 12H, -CH(CH_3)$_2$) 1.17 (m, 4H, PCy_3), 1.06 (m, 7H, PCy_3); ^{13}C NMR ($CDCl_3$, ppm): δ 176.33 (-*C*O_2CH_3), 156.92 (*C*=N), 145.69, 144.34, 143.05, 141.86, 138.76, 138.69, 137.48, 134.30, 130.92, 130.88, 127.71, 127.15, 126.27, 122.51, 122.03, 113.94, 100.17, 51.53 (-*C*H$_2$-), 34.03, 33.90, 33.31, 33.15, 30.20, 29.69, 28.11, 28.02, 26.71, 26.56, 25.62, 24.45, 24.36. ^{31}P NMR ($CDCl_3$, ppm) δ 33.16. HRMS *m/z* calcd for $C_{46}H_{63}N_2O_2PPd$: 812.3662 [M], 753.3529 [M-OAc]$^+$ found 753.3557 [M-OAc]$^+$

[Pd(N,N'-di(p-acetophenyl)-2-iminoisoindoline)(OAc)PCy_3] (10)

Compound **10** was obtained as a yellow powder in 78% yield from palladacycle **4** (228 mg, 0.214 mmol) and tricyclohexylphosphine (126 mg, 0.449 mmol) using procedure A. ^{1}H NMR ($CDCl_3$, ppm) δ 8.15 (m, 1H, Ar), 7.90 (d, *J* = 8.1, 2H, Ar), 7.63 (d, *J* = 8.2, 1H, Ar), 7.51 (d, *J* = 7.4, 1H, Ar), 7.45 (m, 1H, Ar), 7.27 (d, *J* = 8.1, 2H, Ar), 7.05 (m, 1H, Ar), 6.92 (d, *J* = 8.4, 1H, Ar), 6.31 (d, *J* = 8.1, 2H, Ar), 5.16 (s, 2H, -C*H*$_2$-), 2.60 (s, 3H, -C(=O)C*H*$_3$), 2.53 (s, 3H, -C(=O)C*H*$_3$), 2.01 (m, 3H, PCy_3), 1.83 (m, 6H, PCy_3), 1.71 (m, 6H, PCy_3), 1.62 (m, 3H, PCy_3), 1.53 (s, 3H, -CO_2CH_3), 1.48 (m, 6H, PCy_3), 1.15 (m, 3H, PCy_3), 1.04 (m, 6H, PCy_3); ^{13}C NMR ($CDCl_3$, ppm): δ 197.90 (-*C*(=O)CH_3), 197.78 (-*C*(=O)CH_3), 176.47 (-*C*O_2CH_3), 157.03 (-C=N-), 150.99, 143.09, 141.86, 141.63, 141.56, 134.86, 134.17, 132.44, 132.42, 132.00, 130.05, 130.00, 128.25, 127.21, 126.43, 124.90, 122.91, 114.04, 52.21, 33.55, 33.38, 29.79, 28.13, 28.05, 26.89, 26.87, 26.63, 25.42; ^{31}P NMR ($CDCl_3$, ppm) δ 35.16. Elemental analysis (%) calcd. for $C_{44}H_{55}N_2O_4PPd\cdot(CH_2Cl_2)_{0.3}$: C 63.43, H 6.68, N 3.34; found: C 63.47, H 6.51, N 3.27 (^{1}H NMR

analysis of the sample showed presence of 0.3 equiv of CH_2Cl_2 which was used as the crystallization solvent). HRMS *m/z* calcd for $C_{44}H_{55}N_2O_4PPd$: 812.2934 [M], 753.2801 $[M\text{-}OAc]^+$ found 753.2754 $[M\text{-}OAc]^+$.

General procedure (B) for synthesis of [Pd(iminoisoindoline)(Cl)PR_3] complexes 11-14.

A flask was charged with [Pd(iminoisoindoline)(μ-OAc)]$_2$ and excess (20 equiv) LiCl in acetone and the mixture was stirred for 12 h. The resulting yellow precipitate was isolated, washed with water then acetone and dried under vacuum. The resulting yellow powder was then suspended in dichloromethane. Palladacycles **11-14** were obtained by the reaction of the yellow suspension with equimolar amounts of phosphine (PPh_3 or PCy_3) at room temperature. Over the course of 12 h with stirring, the yellow suspension gradually became a clear colourless solution. The resulting solution was filtered and the filtrate was concentrated to circa 2 mL. Hexanes were then added to precipitate out the desired complex, which was filtered, washed with 3x10 mL of hexanes, then dried under vacuum. Single crystals of palladacycles **12** and **13** were obtained from slow evaporation of a concentrated dichloromethane/hexane (1:1) solution.

Synthesis of [Pd(N,N'-diphenyl-2-iminoisoindoline)(Cl)PPh_3] (11)

(84.0%, yellow powder). ^{1}H NMR ($CDCl_3$, ppm) δ 7.56 (m, 7H, Ar), 7.48 (m, 3H, Ar), 7.41 (m, 1H,Ar), 7.29 (m, 6H, Ar), 7.22 (m, 5H, Ar), 7.03 (m, 1H, Ar), 6.80 (m, 3H, Ar) 6.15 (m, 2H, Ar), 5.15 (s, 2H, -C*H*$_2$-); ^{13}C NMR ($CDCl_3$, ppm): δ 157.65 (-C=N-), 147.03, 141.98, 141.77, 141.67, 137.32, 136.86, 135.30, 135.21, 132.28, 131.90, 131.33, 131.00, 130.00, 128.22, 128.08, 128.00, 127.71, 127.16, 125.99, 123.98, 123.85, 122.62, 51.46 (-*C*H$_2$-). ^{31}P NMR ($CDCl_3$, ppm) δ 34.81. Elemental analysis (%) calcd. for $C_{38}H_{30}ClN_2PPd$: C 66.39, H 4.40, N 4.07; found: C

66.56, H 4.42, N 3.93. HRMS *m/z* calcd for $C_{38}H_{30}ClN_2PPd$: 686.0870 [M], 651.1181 $[M\text{-}Cl]^+$ found 651.1194 $[M\text{-}Cl]^+$.

Synthesis of [Pd(N,N'-diphenyl-2-iminoisoindoline)(Cl)PCy_3] (12)

(80.0%, yellow powder). ^1H NMR ($CDCl_3$, ppm) δ 7.49 (m, 3H, Ar), 7.40 (m, 1H, Ar), 7.24 (m, 3H, Ar), 7.16 (m, 1H, Ar), 7.03 (m, 2H, Ar), 6.92 (m, 1H, Ar), 6.85 (d, *J* = 7.8, 1H, Ar), 6.31 (d, *J* = 8.1, 1H, Ar), 5.11 (s, 2H, -CH_2-), 2.21 (m, 3H, PCy_3), 1.84 (m, 6H, PCy_3), 1.69 (m, 6H, PCy_3), 1.56 (m, 9H, PCy_3), 1.19 (m, 3H, PCy_3), 1.05 (m, 6H, PCy_3); ^{13}C NMR ($CDCl_3$, ppm): δ 159.00 (-C=N-), 147.27, 142.43, 139.87, 139.81, 139.64, 138.66, 131.27, 130.75, 130.73, 128.21, 128.02, 127.27, 127.15, 125.56, 124.59, 124.56, 124.11, 122.72, 114.16, 50.84 (-CH_2-), 34.54 (PCy_3), 34.36 (PCy_3), 30.17 (PCy_3), 28.04 (PCy_3), 27.96 (PCy_3), 26.74 (PCy_3). ^{31}P NMR ($CDCl_3$, ppm) δ 34.99. Elemental analysis (%) calcd for $C_{38}H_{48}ClN_2PPd$: C 64.68, H 6.86, N 3.97; found: C 64.53, H 6.49, N 3.97. HRMS *m/z* calcd for $C_{38}H_{48}ClN_2PPd$: 704.2 [M], 669.3 $[M\text{-}Cl]^+$ found 669.3 $[M\text{-}Cl]^+$.

Synthesis of [Pd(N,N'-di(p-acetophenyl)-2-iminoisoindoline)(Cl)PPh_3] (13)

(78.0%, yellow powder). ^1H NMR ($CDCl_3$, ppm) δ 7.95 (d, *J* = 8.6, 2H, Ar), 7.56 (m, 9H, Ar), 7.53 (m, 1H, Ar), 7.42 (m, 2H, Ar), 7.31 (m, 3H, Ar), 7.23 (m, 6H, Ar), 7.07 (m, 1H, Ar), 6.91 (d, *J* = 8.7, 1H, Ar), 6.31 (d, *J* = 8.7, 1H, Ar), 5.21 (s, 2H, -CH_2-), 2.60 (s, 3H, -C(=O)CH_3), 2.01 (s, 3H, -C(=O)CH_3); ^{13}C NMR ($CDCl_3$, ppm): δ 197.83 (-*C*(=O)CH_3), 197.13 (-*C*(=O)CH_3), 157.55 (-*C*=N), 150.81, 143.16, 143.05, 141.97, 141.05, 135.19, 135.10, 134.91, 132.21, 131.56, 131.16, 130.43, 130.13, 128.8, 128.49, 128.32, 128.23, 127.66, 127.14, 124.55, 122.96, 113.77, 51.91 (-*C*H_2-), 26.87 (-C(=O)*C*H_3), 26.10 (-C(=O)*C*H_3). ^{31}P NMR ($CDCl_3$, ppm) δ 35.70. Elemental analysis (%) calcd. for $C_{42}H_{34}ClN_2O_2PPd\cdot(CH_2Cl_2)$: C 60.30, H 4.24, N 3.27; found: C

60.87, H 3.92, N 3.45. HRMS *m/z* calcd for $C_{42}H_{34}ClN_2O_2PPd$: 770.1081 [M], 735.1393 $[M\text{-}Cl]^+$ found 735.1400 $[M\text{-}Cl]^+$.

Synthesis of [Pd(N,N'-di(p-acetophenyl)-2-iminoisoindoline)(Cl)PCy_3] (14)

(90.0%, pale yellow powder). ^1H NMR ($CDCl_3$, ppm) δ 8.17 (s, 1H, Ar), 7.90 (d, *J* = 8.4, 2H, Ar), 7.67 (d, *J* = 8.4, 1H, Ar), 7.54 (m, 4H, Ar), 7.09 (m, 1H, Ar), 6.94 (d, *J* = 8.4, 1H, Ar), 6.47 (d, *J* = 8.1, 1H, Ar), 5.19 (s, 2H, -C*H*$_2$-), 2.59 (s, 3H, -C(=O)C*H*$_3$), 2.55 (s, 3H, -C(=O)C*H*$_3$), 2.18 (m, 3H, PCy_3), 1.85 (m, 6H, PCy_3), 1.69 (m, 6H, PCy_3), 1.55 (m, 9H, PCy_3), 1.19 (m, 3H, PCy_3), 1.05 (m, 6H, PCy_3).; ^{13}C NMR ($CDCl_3$, ppm): δ197.84 (-*C*(=O)CH_3), 197.53(-*C*(=O)CH_3), 158.72 (-*C*=N-), 150.96, 143.26, 142.33, 140.71, 140.65, 138.48, 134.47, 133.64, 132.16, 129.93, 129.22, 128.75, 128.42, 127.23, 127.14, 125.02, 123.02, 113.97, 51.43(-*C*H_2-), 34.78 (PCy_3), 34.60 (PCy_3), 30.19 (PCy_3), 28.05 (PCy_3), 27.96 (PCy_3), 26.82 (PCy_3), 26.74 (-C(=O)*C*H_3), 26.61 (-C(=O)*C*H_3). ^{31}P NMR ($CDCl_3$, ppm) δ 37.29. Elemental analysis (%) calcd for $C_{42}H_{52}ClN_2O_2PPd$: C 63.88, H 6.64, N 3.55.; found: C 63.76, H 6.77, N 3.54.; HRMS *m/z* calcd for $C_{42}H_{52}ClN_2O_2PPd$: 788.2490 [M], 753.2801 $[M\text{-}Cl]^+$ found 735.2799 $[M\text{-}Cl]^+$.

4.6 X-ray structure determinations

Data were collected at -100 ºC on a Nonius Kappa CCD diffractometer, using the COLLECT program.[26] Cell refinement and data reductions used the programs DENZO and SCALEPACK.[27] SIR97[28] was used to solve the structures and SHELXL97[29] was used to refine the structures. ORTEP-3 for Windows[30] was used for molecular graphics and PLATON[31] was used to prepare material for publication. H atoms were placed in calculated positions with U_{iso}

constrained to be 1.5 times U_{eq} of the carrier atom for methyl protons and 1.2 times U_{eq} of the carrier atom for all other hydrogen atoms.

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4.7 Appendix A. Supplementary material

CCDC 707316-707319 contain the supplementary crystallographic data for **5**, **10•CH_2Cl_2**, **12** and **13•CH_2Cl_2**. The data can be obtained free of charge via http://www.ccdc.cam.ac.uk/conts/retrieving.html, or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: (+44) 1223-336-033; or e-mail: deposit@ccdc.cam.ac.uk.

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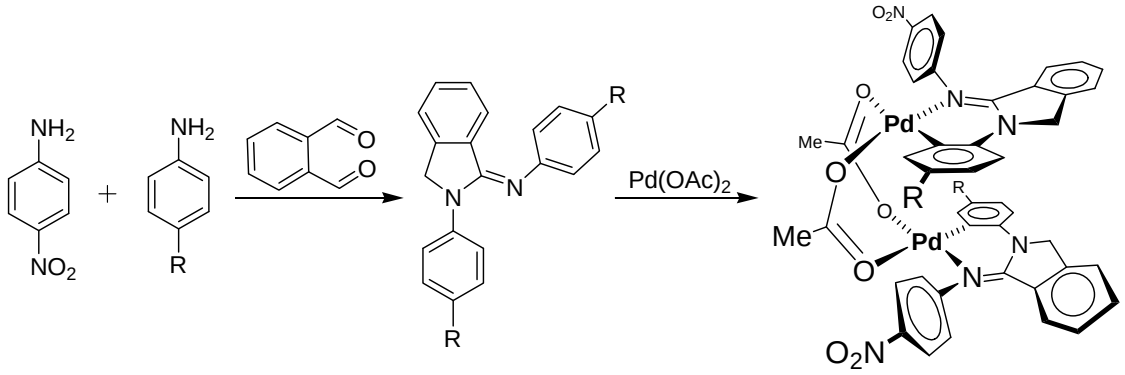
CHAPTER 5

PUBLICATION 4

Description

The following is a submitted manuscript which describes the synthesis and characterization of a series of mixed Ar,Ar'-diaryliminoisoindoline ligands and their corresponding six-membered dinuclear palladacycles of the general formula [(Ar,Ar'-diaryliminoisoindoline)Pd{μ-OAc}]$_2$. The ligands were prepared through a one-step three-component reaction from commercially available starting materials. All complexes (**5-8**) were synthesized and characterized by standard methods and their molecular structures determined by single crystal X-ray analysis.



Authors' Contribution

I synthesized and fully characterized all mixed-iminoisoindoline ligands (**1-4**) and their corresponding mononuclear palladacycles (**5-8**). Dr. J. Wilson Quail did all the structure determination by single crystal X-ray analysis and the work was supervised by Dr. Stephen R. Foley.

Relation of Chapter 5 (Publication 4) to the Objectives of this Project

We noticed from the second research objective (see Chapter 3) that the iminoisoindoline ligand obtained from the reaction of phthaladehyde with *p*-nitroaniline was unreactive towards Pd(II) precursors. This was attributed to reduced electron density on the imine nitrogen due to the highly electron withdrawing ability of the nitro group on the *para*-position of the benzene rings.

Therefore, we were interested in selectively synthesizing "mixed" diaryliminoisoindolines where the aryl group on the imine nitrogen would contain a nitro group while the other aryl moiety on the nitrogen in the iminoisoindoline ring would contain an aryl group with a more electron donating substituent. Could a palladacycle now be formed with only one nitro substituent? If so, how would this affect C-C coupling activity?

Consequently, a series of "mixed" *Ar,Ar'*-diaryl-2-iminoisoindolines [Ar ≠ Ar' = *p*-NO_2-C_6H_3] ligands were synthesized by reacting equimolar amounts of phthaladehyde, *p*-nitroaniline and *p*-R-aniline (R = H, Me, MeO, ^{i}Pr) in one-pot synthesis. The desired compounds precipitated out of solution as analytically pure solids and interestingly, formation of dinuclear palladacycles was now observed.

5. Synthesis of mixed Ar,Ar'-Diaryliminoisoindolines for Applications in formation of Palladacycle

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5.1 Abstract

The synthesis of Ar,Ar'-diaryliminoisoindolines containing different aryl groups bound to the two nitrogen atoms is described. The iminoisoindolines were obtained by a one-pot reaction of phthalaldehyde with 1 equiv *p*-NO_2-aniline and 1 equiv *p*-R-aniline, where R = H, Me, MeO or ^{i}Pr, resulting in formation of non-symmetrically substituted iminoisoindolines, 1-*p*-nitrophenylimino-2-*p*-R-phenylisoindoline (R = H (**1**), Me (**2**), MeO (**3**), ^{i}Pr (**4**)), as analytically pure precipitates requiring no further purification. Only one conformer precipitates from solution wherein the nitro group resides exclusively at the imine position while the more electron donating substituent ends up on the isoindoline ring position. Reaction of mixed iminoisoindoline ligands with $Pd(OAc)_2$ in dichloromethane at room temperature results in formation of six-membered [C,N] dinuclear cyclopalladated complexes with the general formula [(Ar,Ar'-diaryliminoisoindoline)Pd{μ-OAc}]$_2$ (**5-8**).

5.2 Introduction

Carbon-carbon (C-C) coupling reactions are among the most important transformations in organic synthesis. Palladium based catalysts, in particular palladacycles, have been found to be superior catalytic systems in this regard due to their ease of preparation, air and moisture stability, low loading and high activity.[1] Palladacycles have been known since the 1960s but were not used for C-C coupling reactions until 1995 and have rapidly emerged as being among the most active catalysts known for a large variety of coupling reactions.[2-6] There is a large diversity of palladacycles reported in the literature, the most common of which are palladacycles incorporating [C,P] and [C,N] metallacyclic formations.[7-13] The Pd-C bonds in palladacycles are most commonly formed by intramolecular C-H activation in the *ortho* position of a proximal aryl group to form the metal-carbon bond usually resulting in five- or six-membered ring palladacycles. Several palladacycles are even commercially available from chemical companies such as Aldrich and Strem; most notably the diimine-based Nájera catalyst,[11, 14] the amine-based Indolese catalyst[15] and Bedford's phosphite-based catalyst.[16]

While *N*,*N*'-diaryliminoisoindolines were first synthesized in 1910, few applications have been found for this subclass of indolines, either as ligands or as organic substrates.[17] For example, a SciFinder structure search reveals only 18 independent references in the last 100 years. This is likely due to the fact that diaryliminoisoindolines have not been found as a subunit of any natural products.

We recently reported the synthesis of a series of air and moisture stable *N*,*N*'-diaryliminoisoindoline-based palladacycles (Figure 5.1). The iminoisoindoline ligands were easily prepared in one step from the reaction of phthalaldehyde and 2 equiv of the respective aniline. The corresponding palladacycles also required only one step and precipitate from solution as analytically pure solids. These complexes were found to be active pre-catalysts in the

activation of aryl chlorides for the formation of biphenyls and cinnamates in the Suzuki and the Heck coupling reactions, respectively.[18] We further reported that with 1-*p*-nitrophenylimino-2-*p*-nitrophenylisoindoline (R = R' = NO_2; Figure 5.1), there was no reaction with palladium precursors and thus no formation of the corresponding palladacycle. This is likely due to the electron withdrawing/deactivating effects of the nitro substituent inhibiting both imine coordination and *ortho*-palladation. Intrigued by this result, we decided to investigate the synthesis of mixed Ar,Ar'-diaryliminoisoindoline ligands containing different aryl groups bound to the two nitrogen atoms (R ≠ R', Figure 5.1) wherein the aryl groups of the mixed diaryliminoisindoline would contain alternatively one nitro group and one neutral or electron donating group in the *para* positions. Herein we report the synthesis and characterization of a series of mixed Ar,Ar'-diaryliminoisoindolines and subsequent formation of the corresponding air and moisture stable iminoisoindoline-based palladacycles in a simple two-step protocol.

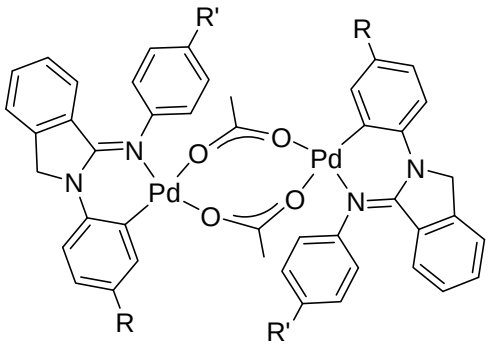


Figure 5.1. Mixed iminoisoindoline-based palladacycles (R ≠ R').

5.3 Results and discussion

5.3.1 Ligand Synthesis

As we have previously reported, the diaryliminoisoindoline, 1-*p*-nitrophenylimino-2-*p*-nitrophenylisoindoline (R = R' = NO_2; Figure 5.1), did not react with palladium precursors to form the corresponding palladacycle. This is likely due to the highly electron withdrawing nature of the nitro substituents inhibiting *ortho*-palladation. We envisioned that substitution of the nitro group of the aryl ring bound directly to the isoindoline skeleton with more electron donating substituents would allow for C-H activation and subsequent palladacycle formation. As with the previously reported symmetrically substituted iminoisoindolines, the non-symmetrically substituted ligands proved remarkably easy to synthesize. The one pot reaction of phthalaldehyde with 1 equiv *p*-NO_2-aniline and 1 equiv *p*-R-aniline, where R = H, Me, MeO or ^{i}Pr, results in successful formation of non-symmetrically substituted iminoisoindoline ligands (R = H (**1**), Me (**2**), MeO (**3**), ^{i}Pr (**4**)) in 40-55% yield as shown in Schemes 5.1 and 5.2. In compounds **1**-**4**, the nitro group resides exclusively at the imine position while the more electron donating substituent ends up on the isoindoline ring position. The desired compounds precipitated out of solution as analytically pure, yellow solids. The mixed iminoisoindolines are all previously unreported except for **3**.[19] Compounds **1**-**4** were characterized by ^{1}H and ^{13}C NMR, mass spectrometry, elemental analysis and IR spectroscopy. ^{1}H NMR spectra show a characteristic singlet for the CH_2 moiety of the isoindoline ring of **1**-**4** at ~5 ppm and the C=N stretching frequency in the IR spectra appears at ~1645 cm^{-1}.

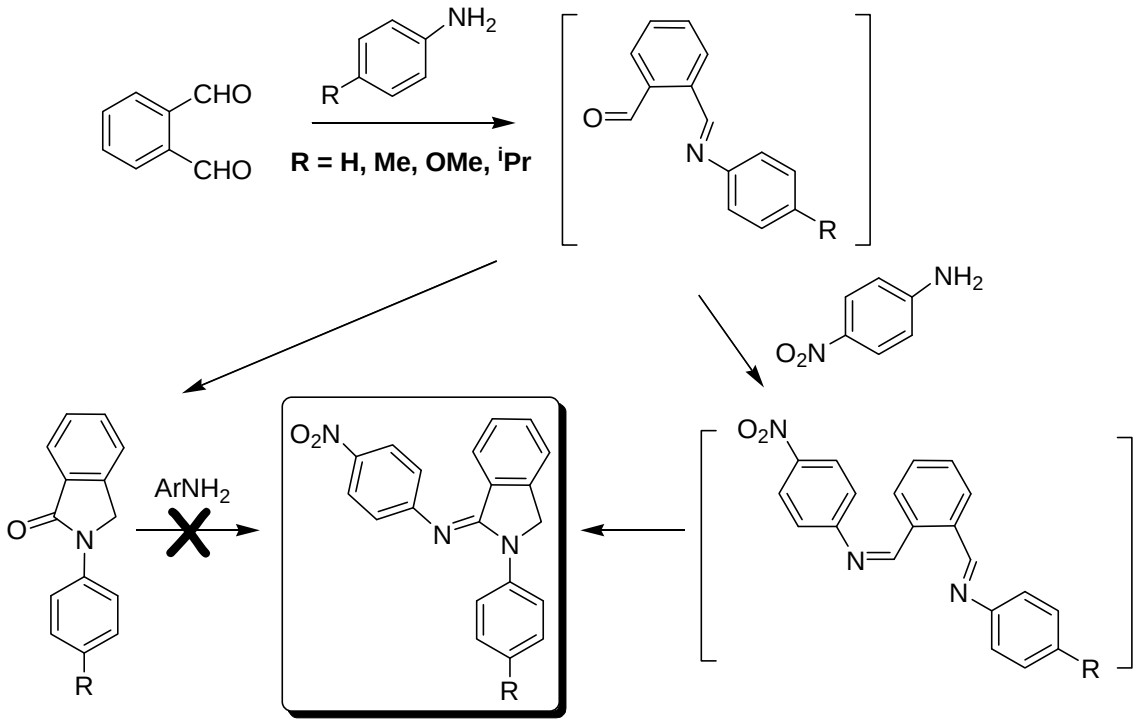
The mixed Ar,Ar'-diaryliminoisoindoline synthesis likely proceeds first via reaction of phthalaldehyde with one equiv of the more electron donating aniline resulting in formation of an imino-aldehyde (Scheme 1). The resulting imino-aldehyde can then undergo a slower second

condensation reaction with *p*-NO_2-aniline forming a transient γ-diimine. The γ-diimine then undergoes intramolecular cyclization initiated by the more electron donating imine to form the corresponding iminoisoindoline with the NO_2 moiety exclusively on the imine position. We have previously shown that the γ-diimine intermediate can only be isolated providing the aryl groups are sufficiently bulky to inhibit intramolecular cyclization.[20] A competing side reaction also occurs where intramolecular cyclization of the transient imino-aldehyde species results in formation of the corresponding isoindolinone which limits the overall yield of the mixed iminoisoindoline ligands. The presence of the isoindolinone was confirmed by MS analysis of the filtrate. Fortuitously, under the reaction conditions employed, the isoindolinone remains in solution while the desired iminoisoindoline precipitates out as a yellow powder. The isoindolinone does not further react with $ArNH_2$ (Scheme 5.1).

Unlike the diaryliminoisoindolines, the corresponding *N*-arylisoindolinones have found widespread application in the pharmaceutical industry with many examples being commercially available including the isoindolinones from Scheme 5.1.[21, 22] Recent publications by the groups of Pan as well as Alajarín and Sánchez-Andrada provide mechanistic details into the formation of isoindolinones from phthaldehyde.[23, 24]

When the reaction is carried out with two different anilines both bearing electron withdrawing groups in the *para* position (specifically NO_2 and COMe), the resulting iminoisoindoline precipitates as a mixture of three compounds: 1-*p*-nitrophenylimino-2-*p*-acetylphenylisoindoline (**A**), 1-*p*-acetylphenylimino-2-*p*-acetylphenylisoindoline (**B**) and 1-*p*-nitrophenylimino-2-*p*-nitrophenylisoindoline (**C**) in the ratio 17:5:1, respectively as shown in Scheme 5.3 in 80 % overall yield. Compounds **A**-**C** were identified by mass spectrometry as well as ^1H and ^{13}C NMR spectroscopy. Compounds **B** and **C** have been previously reported,[18, 19] while

characterization of **A** is herein reported. Thus it appears that in order to facilitate isolation of a mixed iminoisoindoline in a one-pot synthesis, a significant difference in the electron donating ability of the two *para*-substituted anilines must be employed.

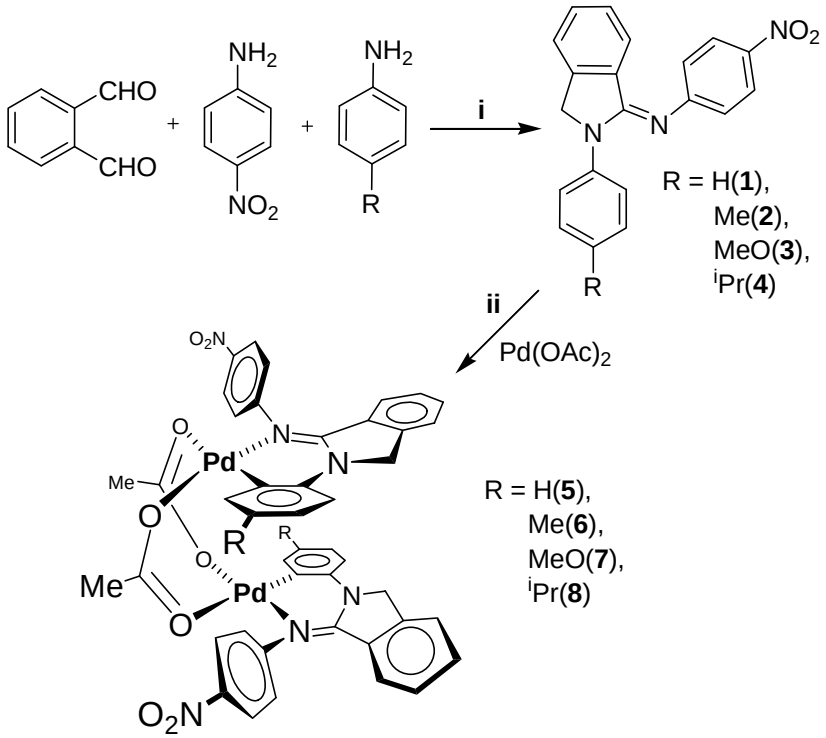


Scheme 5.1. Synthesis of mixed Ar,Ar'-diaryliminoisoindolines.

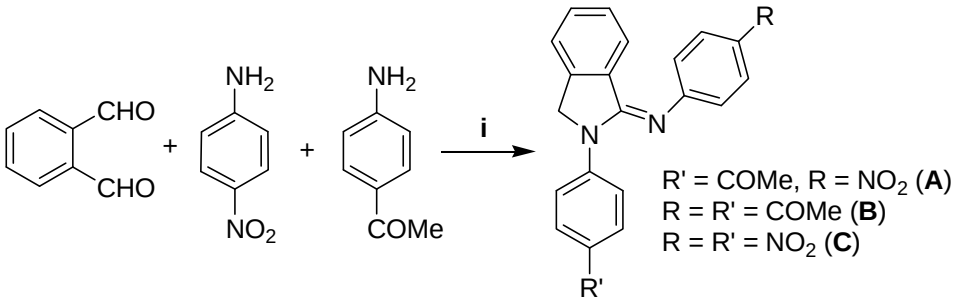
5.3.2 Synthesis of [(mixed-iminoisoindoline)Pd{μ-OAc}]$_2$ palladacycles

Reaction of $Pd(OAc)_2$ in dichloromethane at ambient temperature, with one equiv of the respective mixed-iminoisoindoline **1-4** resulted in formation of acetato-bridged, dinuclear palladacyclic complexes **5-8** as analytically pure, yellow solids of the general formula, [(iminoisoindoline)Pd(μ-OAc)]$_2$ (Scheme 5.2). As mentioned earlier, no palladacycle was obtained from reaction of 1-*p*-nitrophenylimino-2-*p*-nitrophenylisoindoline (**C**) and $Pd(OAc)_2$.

Substitution of one nitro group on the ring position of **C** with a more electron donating substituent results in successful formation of air and moisture stable mixed-iminoisoindoline palladacycles **5-8**.



Scheme 5.2. Preparation of mixed-iminoisoindoline ligands and their corresponding palladacycles. i) methanol:ether (1:1) as solvent, formic acid, ambient temperature, 12 h. ii) CH_2Cl_2 as solvent, ambient temperature, 12 h.



Scheme 5.3. Synthesis of mixed iminoisoindoline ligands from two substituted anilines which both contain electron withdrawing groups. i) methanol:ether (1:1) as solvent, formic acid, ambient temperature, 12 h.

Palladacycles **5-8** were characterized by IR and NMR spectroscopy, mass spectrometry and elemental analysis. Crystal structures were also obtained for all palladacycles to further confirm the coordination environment around the metal centers.

In the IR spectra of complexes **5-8**, the signals for the C=N bond vibrations were shifted to lower wavenumber compared to those of the free iminoisoindoline (Δ(wavenumber) ~ 35 cm^{-1}) consistent with the formation of a Pd-N bond in the cyclopalladated complexes. Elemental analysis data for all complexes are consistent with the proposed acetate-bridged dinuclear structures.

Dinuclear palladacycles in which the two palladium centers are linked by two bridging acetato groups can exhibit *anti*- and *syn*-isomerization.[18, 25-30] In this case, NMR data allows for easy differentiation between the *anti*- and *syn*-conformations where the *anti*-isomer exhibits overall C_2 symmetry and the *syn*-isomer is C_s symmetric. A characteristic indication of cyclopalladation in complexes **5-8** is the observed ^{1}H NMR resonance for the CH_2 protons of the iminoisoindoline ring. The ligands (**1-4**) show a singlet corresponding to the two methylene protons at ~5 ppm. Upon cyclopalladation, these methylene protons become diastereotopic in the

anti-isomer resulting in formation of two doublets at ~4.6 and ~3.5 ppm, each corresponding to one proton per ligand. Due to steric effects in all four complexes, only the *anti*-isomer was obtained. The ESI-Q-TOF mass spectra of complexes **5-8** all showed a distinct signal which was assigned to their respective molecular cation $[M\text{-}OAc]^+$.

X-ray diffraction studies were undertaken and the crystal structures of palladacycles **5-8** were determined. Complex **5** co-crystallized with one molecule of chloroform, the solvent of crystallization, while **6** had two unsymmetrical molecules along with water and dichloromethane in the unit cell. **6** was crystallized under air from dichloromethane which had not been previously dried. All four complexes crystallized exclusively as the *anti*-isomer, unambiguously confirming the presence of a six-membered [C,N] palladacycle. The *anti*-configuration is also observed in the crystal structures of most of the previously reported acetato-bridged dinuclear palladacycles.[18] The two palladium atoms are bridged by two acetato ligands with each palladium center having a chelating [C,N]-bound iminoisoindoline ligand forming the palladacycle. The dinuclear acetato-bridged complexes adopt a characteristic closed-book conformation where the two [C,N]-bound iminoisoindoline ligands stack on top of one another. As expected, the coordination geometry about the palladium atoms in all four structures is approximately square planar with the sum of the angles around the palladium atoms for all three complexes being 360±1°. The Pd-Pd distance was found to be 3.1109(6) Å for **5**, 2.9856(6) Å for **6**, 3.0449(6) for **7** and 3.0453(4) Å for **8** which is consistent with previously reported acetato-bridged dinuclear palladacycles.[18] The Pd-C and Pd-N bond lengths of complexes **5-8** were all essentially identical (within esd) at 1.97(1) Å and 2.01(1) Å respectively. The Pd–O distances of the two acetate ligands differ by about 0.10 Å for **5-8** (for example, in **6**, Pd(1)-O(1) is 2.137 Å while Pd(1)-O(3) is 2.063 Å), indicative of the stronger trans-influence of the metallated carbon compared to that of the imine nitrogen.

ORTEP plots for **5-8** are shown in Figures 5.2 through 5.5 with bond distances and angles indicated in their respective captions. Crystallographic data and refinement parameters are summarized in Table 5.1.

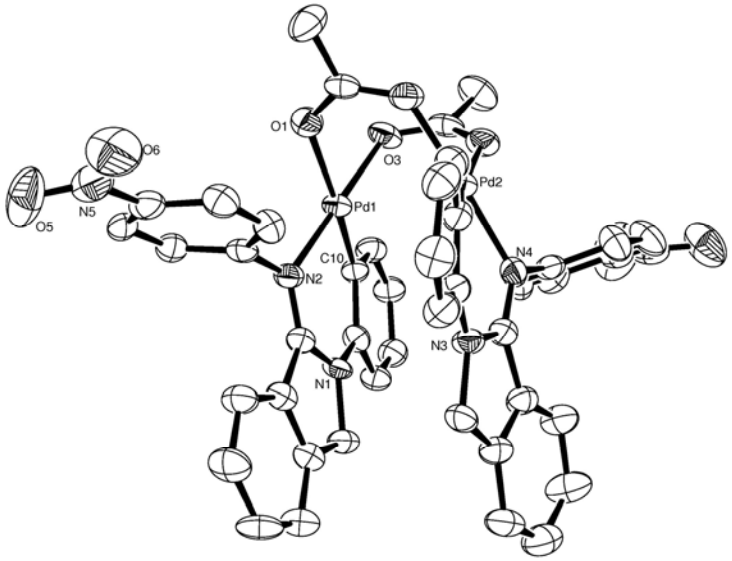


Figure 5.2. ORTEP plot of **5** at the 50% probability level. The hydrogen atoms and $CHCl_3$ molecule have been omitted for clarity. Selected bond lengths [Å] and angles [^{o}]: Pd(1)-C(10) = 1.967(6), Pd(1)-N(2) = 2.006(5), Pd(1)-O(3) = 2.063(5), Pd(1)-O(1) = 2.138(4), Pd(1)-Pd(2) = 3.1109(6), C(10)-Pd(1)-N(2) = 89.6(2), C(10)-Pd(1)-O(3) = 90.6(2), N(2)-Pd(1)-O(1) = 94.05(19), N(2)-Pd(1)-O(3) = 179.34(18), O(3)-Pd(1)-O(1) = 85.75(18).

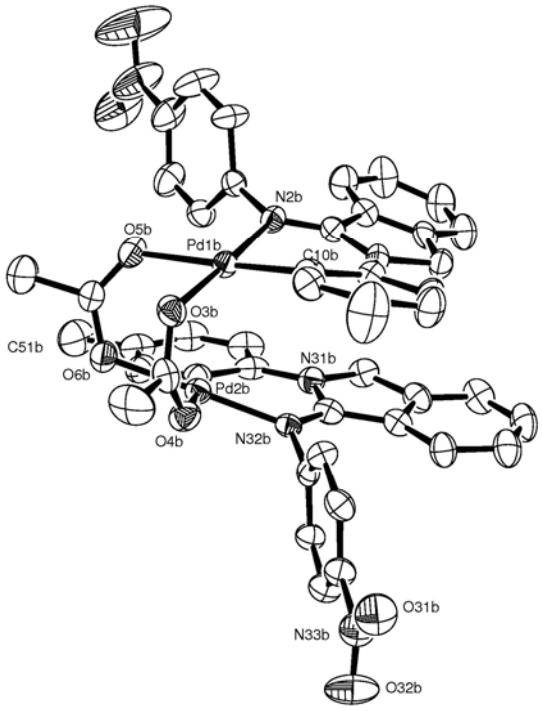


Figure 5.3. ORTEP plot of **6** (view of molecule B) at the 30% probability level. Hydrogen atoms, molecule A and solvent molecules have been omitted for clarity. Selected bond lengths [Å] and angles [^{o}]: Pd(1B)-C(10B) = 1.968(6), Pd(1B)-N(2B) = 2.004(5), Pd(1B)-O(3B) = 2.058(4), Pd(1B)-O(1B) = 2.140(4), Pd(1B)-Pd(2B) = 2.9856(6), C(10B)-Pd(1B)-N(2B) = 89.0(2), C(10B)-Pd(1B)-O(3B) = 91.5(2), N(2B)-Pd(1B)-O(5B) = 178.25(18), N(2B)-Pd(1B)-O(1B) = 93.70(18), O(3B)-Pd(1B)-O(1B) = 85.62(17)

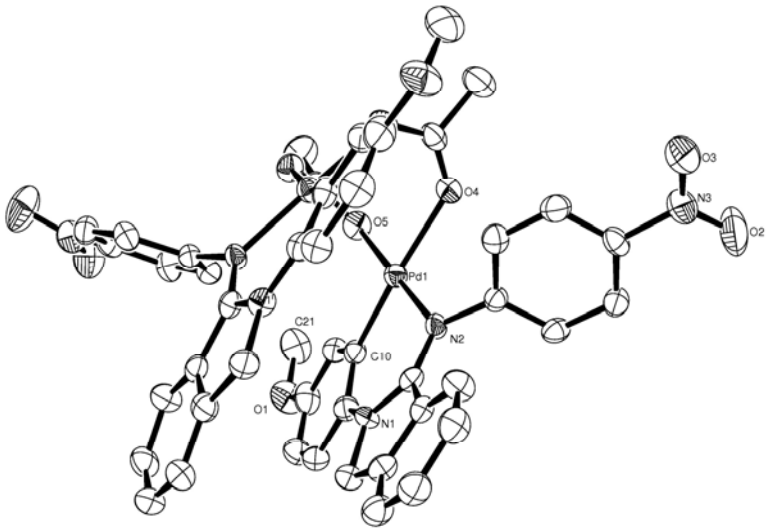


Figure 5.4. ORTEP plot of **7** at the 50% probability level. The hydrogen atoms have been omitted for clarity. Selected bond lengths [Å] and angles [^{o}]: Pd(1)-C(10) = 1.974(6), Pd(1)-N(2) = 2.011(5), Pd(1)-O(3) = 2.060(4), Pd(1)-O(1) = 2.137(4), Pd(1)-Pd(2) = 3.0444(9), C(10)-Pd(1)-N(2) = 89.7(2), C(10)-Pd(1)-O(3) = 91.5(2), N(2)-Pd(1)-O(1) = 95.89(17), N(2)-Pd(1)-O(3) = 178.48(18), O(3)-Pd(1)-O(1) = 82.99(17).

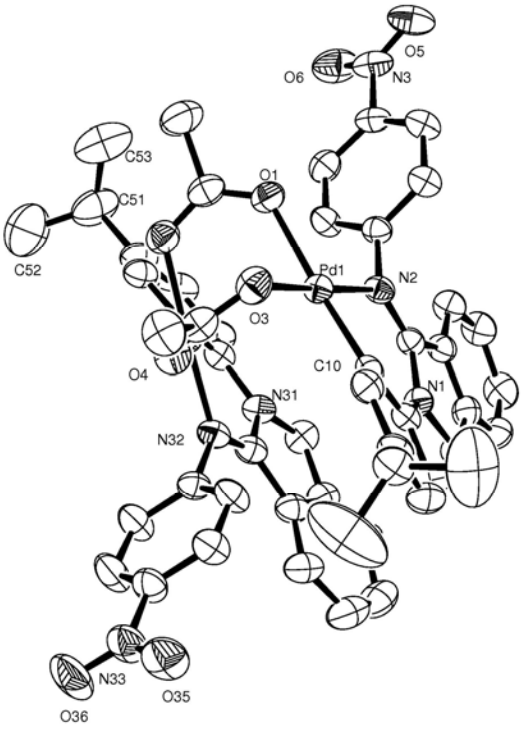


Figure 5.5. ORTEP plot of **8** at the 30% probability level. The hydrogen atoms have been omitted for clarity. Selected bond lengths [Å] and angles [°]: Pd(1)-C(10) = 1.964(4), Pd(1)-N(2) = 2.012(3), Pd(1)-O(3) = 2.057(3), Pd(1)-O(1) = 2.133(3), Pd(1)-Pd(2) = 3.0453(3), C(10)-Pd(1)-N(2) = 89.92(15), C(10)-Pd(1)-O(3) = 90.29(14), N(2)-Pd(1)-O(5) = 178.18(14), N(2)-Pd(1)-O(1) = 93.11(12), O(3)-Pd(1)-O(1) = 86.50(12)

Table 5.1. Crystal data and refinement parameters for complexes **5**·$CHCl_3$, **6**·$1.5H_2O$·$0.75CH_2Cl_2$, **7** and **8.**

	5·$CHCl_3$	**6**·$1.5H_2O$·$0.75CH_2Cl_2$	**7**	**8**
Formula	$C_{44}H_{35}Cl_3N_6O_8Pd_2$	$C_{187}H_{170}Cl_6N_{24}O_{38}Pd_8$	$C_{46}H_{38}N_6O_{10}Pd_2$	$C_{50}H_{46}N_6O_8Pd_2$
Fw	1106.94	4425.37	1047.62	1071.77
Color	Pale yellow	Yellow	Orange	Yellow
Crystal size, mm^3	0.12 x 0.10 x 0.09	0.12 x 0.10 x 0.10	0.15 x 0.13 x 0.05	0.20 x 0.18 x 0.10
Crystal system	Triclinic	Orthorhombic	Tetragonal	Monoclinic
Space group	P-1	P21 21 2	P41 21 2	P21/c
a, Å	11.7500(4)	20.4831(3)	9.2363(13)	12.7855(2)
b, Å	12.0285(6)	21.2390(3)	9.2363(13)	17.2702(4)
c, Å	17.2210(8)	23.8327(3)	47.882(10)	23.0660(5)
α, deg	107.308(2)	90	90	90
β, deg	109.238(3)	90	90	120.0295(14)
γ, deg	91.590(3)	90	90	90
Z	2	2	4	4
ρ_{calc}, Mg m^{-3}	1.692	1.418	1.704	1.429
T, K	173(2)	173(2)	173(2)	173(2)
Collec./Ind. Ref.	27459/7655	101049/18295	27158/3605	47210/9856
R(int)	0.1114	0.0890	0.1095	0.0947
F(000)	1108	4468	2112	2176
θ range, deg	2.39 to 25.10	2.20 to 25.03	1.70 to 25.03	2.16 to 26.10
FinalR_1(I >2σI)	R1 = 0.0618,	R1 = 0.0444,	R1 = 0.0477,	R1 = 0.0495
	wR2 = 0.1475	wR2 = 0.1032	wR2 = 0.0956	wR2 = 0.1182
R_1(all data)	R1 = 0.0861,	R1 = 0.0526,	R1 = 0.0634,	R1 = 0.0631
	wR2 = 0.1652	wR2 = 0.1077	wR2 = 0.1142	wR2 = 0.1256

5.4 Conclusion

Ar,Ar'-diaryliminoisoindolines containing different aryl groups on the two nitrogen atoms were obtained by a one-pot reaction from inexpensive, commercially available starting materials. The aryl groups were chosen to maximize the difference in electron donating character of the substituents. This not only favors formation of the desired mixed iminoisoindolines, wherein the more electron withdrawing substituent resides exclusively on the imine position, but also promotes C_{aryl}-H activation to form air- and moisture-stable palladacyclic complexes in a simple two-step reaction. This is in contrast to the electron-poor iminoisoindoline, 1-*p*-nitrophenylimino-2-*p*-nitrophenylisoindoline, which does not undergo *ortho*-palladation. Catalytic studies of these complexes in the Suzuki and the Heck coupling reactions are currently ongoing in our laboratory and these results will be reported at a later stage.

5.5 Experimental Section

General Information. Unless otherwise stated, all reactions were performed under N_2 using standard Schlenk techniques or in a N_2-filled drybox. ^1H and ^{13}C $\{^1H\}$ NMR spectra were recorded on a Bruker 500 MHz Avance spectrometer. Chemical shifts for ^1H and ^{13}C NMR are reported in ppm in reference to the residual ^1H and ^{13}C resonances of $CDCl_3$ (^1H: δ 7.24; ^{13}C: δ 77.23). Coupling constants are given in Hz. Elemental analyses were performed on a Perkin-Elmer 2400 CHN elemental analyzer. High resolution mass spectra (HRMS) were measured on an Applied Biosystem QSTAR® XL MS/MS system (ESI-QTOF). $Pd(OAc)_2$ was purchased from PMO Pty Ltd, Australia. Aniline, *p*-toluidine, *p*-anisidine and *p*-isopropylaniline were purchased

from the Sigma-Aldrich Chemical Company and used as received except for aniline which was distilled prior to use. Phthalaldehyde was purchased from Alfa Aesar and used as received.

General Synthesis for ligands A and 1-4

A Schlenk flask was charged with equimolar amounts of the corresponding two substituted anilines in 30 mL methanol:ether (1:1) solvent mixture. Stoichiometric amounts of Phthalaldehyde and 0.05 mL of formic acid were then added. The initially homogeneous solution was stirred at room temperature for 12 h, over which time the product gradually precipitated from solution. The resultant suspension was then filtered and the precipitate washed with cold methanol, and dried under vacuum to obtain the desired product as a white or yellow solid.

1-*p*-nitrophenylimino-2-phenylisoindoline (1)

Compound **1** was obtained as a yellow powder in 47% yield (576 mg) from *p*-NO_2-aniline (517 mg, 3.74 mmol), aniline (349 mg, 3.74 mmol) and phthalaldehyde (502 mg, 3.74 mmol). ^{1}H NMR ($CDCl_3$): δ 8.16 (d, *J* = 9.3, 2H, Ar), 7.80 (d, *J* = 7.4, 2H, Ar), 7.46 (m, 2H), 7.38 (m, 2H), 7.15 (m, 2H), 7.02 (d, *J* = 8.8, 2H), 6.93 (m, 1H), 4.99(s, 2H, CH_2). $^{13}C\{^1H\}$NMR ($CDCl_3$): δ 157.5 ($C_{C=N}$), 153.1(C_{Ar}), 142.7(C_{Ar}), 140.8(C_{Ar}), 140.7(C_{Ar}), 131.6(C_{Ar}), 131.3(CH_{Ar}), 129.3(CH_{Ar}), 128.0(CH_{Ar}), 125.9(CH_{Ar}), 125.4(CH_{Ar}), 124.6(CH_{Ar}), 123.2(CH_{Ar}), 121.8(CH_{Ar}), 121.3(CH_{Ar}), 54.1(>CH_2). Anal. Calcd for $C_{20}H_{15}N_3O_2$: C 72.94; H 4.59; N 12.76. Found: C 72.78; H 4.53; N 12.57. FT-IR (KBr, cm^{-1}): 1654 (C=N), 1589, 1590, 1498, 1469. HRMS *m/z* calcd. for $C_{21}H_{17}N_3O_3$: 329.1164[M], found: 328.1096 $[M-H]^+$.

1-*p*-nitrophenylimino-2-*p*-methylphenylisoindoline (**2**)

Compound **2** was obtained as a yellow powder in 55% yield (711 mg) from *p*-NO_2-aniline (517 mg, 3.74 mmol), *p*-Me-aniline (401 mg, 3.74 mmol) and phthalaldehyde (502 mg, 3.74 mmol). ^{1}H NMR ($CDCl_3$): δ 8.14 (d, *J* = 8.7, 2H, Ar), 7.63 (d, *J* = 7.7, 2H, Ar), 7.46 (m, 2H), 7.17 (m, 3H), 7.00 (d, *J* = 8.7, 2H), 6.95 (m, 1H), 4.99(s, 2H, >CH_2), 2.32(s, 3H, Ar-CH_3. ^{13}C{^{1}H}NMR ($CDCl_3$): δ 157.7 ($C_{C=N}$), 153.2(C_{Ar}), 142.6(C_{Ar}), 140.8(C_{Ar}), 138.2(C_{Ar}), 134.6(C_{Ar}), 131.7(CH_{Ar}), 131.1(CH_{Ar}), 129.9(CH_{Ar}), 127.9(CH_{Ar}), 125.8(CH_{Ar}), 125.4(CH_{Ar}), 123.2(CH_{Ar}), 121.9(CH_{Ar}), 121.8(CH_{Ar}), 121.3(CH_{Ar}), 54.3(>*C*H_2), 21.1 (Ar-*C*H_3). Anal. Calcd. for $C_{21}H_{17}N_3O_2$: C 73.45; H 4.99; N 12.24. Found: C 73.26; H 4.69; N 11.99. FT-IR (KBr, cm^{-1}): 1646 (C=N), 1612, 1584, 1512. HRMS *m/z* calcd. for $C_{21}H_{17}N_3O_2$: 343.1321[M], found: 342.1244$[M-H]^+$.

1-*p*-nitrophenylimino-2-*p*-methoxyphenylisoindoline (**3**)

Compound **3** was obtained as a yellow powder in 42% yield (568 mg) from *p*-NO_2-aniline (521 mg, 3.77 mmol), *p*-MeO-aniline (464 mg, 3.74 mmol) and phthalaldehyde (506 mg, 3.74 mmol). ^{1}H NMR ($CDCl_3$): δ 8.12 (d, *J* = 8.7, 2H, Ar), 7.61 (d, *J* = 8.3, 2H, Ar), 7.46 (m, 2H, Ar), 7.18 (m, 1H, Ar), 6.98 (m, 3H, Ar), 6.90 (d, *J* = 8.8, 2H, Ar), 4.93(s, 2H, >CH_2), 3.78(s, 3H, Ar-OCH_3). ^{13}C{^{1}H}NMR ($CDCl_3$): δ 157.8 ($C_{C=N}$), 157.0(C_{Ar}), 153.4(C_{Ar}), 142.5(C_{Ar}), 140.8(C_{Ar}), 133.7(C_{Ar}), 131.8(C_{Ar}), 131.1(CH_{Ar}), 127.9(CH_{Ar}), 125.8(CH_{Ar}), 125.3(CH_{Ar}), 123.8(CH_{Ar}), 123.2(CH_{Ar}), 121.8(CH_{Ar}), 114.5(CH_{Ar}), 55.7(Ar-O*C*H_3), 54.8(>*C*H_2), Anal. Calcd for $C_{21}H_{15}N_3O_2$: C 70.18; H 4.77; N 11.69. Found: C 70.25; H 4.77; N 11.58. FT-IR (KBr, cm^{-1}): 1643 (C=N), 1581, 1510, 1467. HRMS *m/z* calcd. for $C_{21}H_{17}N_3O_3$: 359.1270 [M], found: 359.1259 [M].

1-*p*-nitrophenylimino-2-*p*-isopropylphenylisoindoline (4)

Compound **4** was obtained as a yellow powder in 42% yield (580 mg) from *p*-NO_2-aniline (516 mg, 3.73 mmol), *p*-^{i}Pr-aniline (505 mg, 3.73 mmol) and phthalaldehyde (502 mg, 3.73 mmol). ^{1}H NMR ($CDCl_3$): δ 8.12 (d, *J* = 8.4, 2H, Ar), 7.65 (d, *J* = 6.6, 2H, Ar), 7.46 (m, 2H), 7.20 (m, 3H), 6.99 (m, 3H), 4.96(s, 2H, >CH_2), 2.88(sept, *J* = 6.9, 1H, CH(CH_3)$_2$), 1.22(d, *J* = 6.9, 6H, CH(CH_3)$_2$). ^{13}C{^{1}H}NMR ($CDCl_3$): δ 157.7 ($C_{C=N}$), 153.2(C_{Ar}), 145.6(C_{Ar}), 142.6(C_{Ar}), 140.8(C_{Ar}), 138.4(C_{Ar}), 131.8(CH_{Ar}), 131.1(CH_{Ar}), 127.9(CH_{Ar}), 127.2(CH_{Ar}), 125.8(CH_{Ar}), 125.3(CH_{Ar}), 123.2(CH_{Ar}), 121.9(CH_{Ar}), 121.8(CH_{Ar}), 54.4(>*C*H_2), 33.9 (CH(CH_3)$_2$), 24.2 (CH(CH_3)$_2$). Anal. Calcd for $C_{23}H_{21}N_3O_2$: C 74.37; H 5.70; N 11.31. Found: C 73.98; H 5.52; N 11.23. FT-IR (KBr, cm^{-1}): 1642 (C=N), 1609, 1583, 1509. HRMS *m/z* calcd. for $C_{23}H_{21}N_3O_2$: 371.1634 [M], found: 370.1544 $[M-H]^+$.

1-*p*-nitrophenylimino-2-*p*-acetylphenylisoindoline (A)

Compound **A** was obtained as a yellow powder in 59% yield (820.0 mg) from *p*-NO_2-aniline (517 mg, 3.74 mmol), *p*-COMe-aniline (506 mg, 3.74 mmol) and phthalaldehyde (502 mg, 3.74 mmol). ^{1}H NMR ($CDCl_3$): δ 8.23 (d, *J* = 8.5, 2H, Ar), 8.06 (d, *J* = 8.6, 2H, Ar), 8.01 (d, *J* = 8.6, 2H, Ar), 7.49 (m, 2H, Ar), 7.14 (m, 1H, Ar), 7.06 (d, *J* = 8.6, 2H, Ar), 6.81 (d, *J* = 7.9, 1H, Ar), 5.03 (s, 2H, >CH_2), 2.58 (s, 3H, -COCH_3). ^{13}C{^{1}H} NMR ($CDCl_3$): δ 196.9 (C_{COMe}), 156.5 ($C_{C=N}$), 152.7 (C_{Ar}), 144.9(C_{Ar}), 143.0(C_{Ar}), 140.1(C_{Ar}), 132.1(C_{Ar}), 131.5(CH_{Ar}), 130.1(C_{Ar}), 129.6(CH_{Ar}), 128.0(CH_{Ar}), 126.0(CH_{Ar}), 125.5(CH_{Ar}), 123.2(CH_{Ar}), 121.2(CH_{Ar}), 118.9(CH_{Ar}), 53.1 (>*C*H_2), 26.5 (CO*C*H_3). HRMS *m/z* calcd. for $C_{22}H_{17}N_3O_3$: 371.1270[M], found: 370.1189 $[M-H]^+$.

5.6 General synthesis for palladacycles 5-8

A Schlenk flask was charged with equimolar amounts of iminoisoindoline (**1**-**4**) and $Pd(OAc)_2$ in dichloromethane (30 mL) to form a reddish homogeneous solution. After 12 h of stirring at ambient temperature under dinitrogen, the reaction mixture was filtered through celite to remove palladium black. The filtrate was concentrated and then ether (30 mL) added to precipitate the desired palladacycles. The resulting precipitates of palladacycles (**5**-**8**) were filtered, washed with cold ether (3x10 mL) then dried under vacuum. Crystals suitable for X-ray diffraction studies were obtained by slow evaporation from a 50:50 dichloromethane/hexane solution under air.

Bis(μ-acetato)bis(1-*p*-nitrophenylimino-2-phenylisoindoline)dipalladium(II) (5).

Complex **5** was obtained as a yellow powder in 27% yield (205 mg) from **1** (252 mg, 0.765 mmol) and $Pd(OAc)_2$ (206 mg, 0.918 mmol). ^{1}H NMR ($CDCl_3$): δ 8.08 (d, *J* = 8.4, 2H, Ar), 7.68 (d, *J* = 7.1, 2H, Ar), 7.55(m, 4H, Ar), 7.35 (d, *J* = 7.5, 2H, Ar), 7.05 (m, 8H, Ar), 6.26 (d, *J* = 7.3, 2H, Ar), 5.79 (m, 8H, Ar), 4.65(d, *J* = 17.2, 2H, C*H*$_2$), 3.27 (d, *J* = 17.2, 2H, C*H*$_2$), 1.66 (s, 6H, acetate); ^{13}C{^{1}H} NMR ($CDCl_3$): δ 180.1 ($C_{acetate}$), 152.0, ($C_{C=N}$), 151.4 (C_{Ar}), 145.7(C_{Ar}), 141.0(C_{Ar}), 136.7 (C_{Ar}) 136.7(CH_{Ar}), 135.7(C_{Ar}), 131.9(CH_{Ar}), 130.3(C_{Ar}), 128.9(CH_{Ar}), 128.7(CH_{Ar}), 127.0(CH_{Ar}), 126.7(CH_{Ar}), 125.6(CH_{Ar}), 124.8(CH_{Ar}), 124.1(CH_{Ar}), 123.1(CH_{Ar}), 122.8(CH_{Ar}), 122.6(CH_{Ar}), 112.5(CH_{Ar}), 53.1(>CH_2), 24.7($CH_{3acetate}$). Anal. calcd (%) for $C_{44}H_{34}N_6O_8Pd_2$: C 53.51; H 3.47; N 8.51 Found: C 52.56; H 3.40; N 7.76; FT-IR (KBr, cm^{-1}) 1618 (C=N), 1562, 1520. HRMS *m/z* calcd. for $C_{44}H_{34}N_6O_8Pd_2$ 987.6162 [M], 929.0379 [M-OAc]$^+$; found 929.0390 [M-OAc]$^+$.

Bis(μ-acetato)bis(1-*p*-nitrophenylimino-2-*p*-methylphenylisoindoline)dipalladium(II) (6).

Complex **6** was obtained as a yellow powder in 36% yield (270 mg) from **2** (254 mg, 0.740 mmol) and $Pd(OAc)_2$ (197 mg, 0.878 mmol). ^1H NMR ($CDCl_3$): δ 8.10 (d, *J* = 8.6, 2H, Ar), 7.66 (d, *J* = 8.8, 2H, Ar), 7.52(m, 2H, Ar), 7.38 (d, *J* = 7.5, 2H, Ar), 7.33(d, *J* = 7.5, 2H, Ar), 7.11(m, 4H, Ar), 6.83(d, *J* = 7.9, 2H, Ar), 6.16 (d, *J* = 8.2, 2H), 5.82 (m, 4H, Ar), 4.61(d, *J* = 17.3, 2H, C*H*$_2$), 3.31 (d, *J* = 17.3, 2H, C*H*$_2$), 2.38 (s, 6H, Ar-CH_3), 1.68 (s, 6H, acetate); $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 180.0 ($C_{acetate}$), 152.2, ($C_{C=N}$), 151.1 (C_{Ar}), 145.6(C_{Ar}), 141.0(C_{Ar}), 136.9 (CH_{Ar}) 136.7(CH_{Ar}), 133.5(C_{Ar}), 133.1(C_{Ar}), 132.5(C_{Ar}), 131.7(CH_{Ar}), 130.4(CH_{Ar}), 129.1(CH_{Ar}), 128.6 (CH_{Ar}), 127.2 (CH_{Ar}), 126.5(CH_{Ar}), 126.2(CH_{Ar}), 124.8(CH_{Ar}), 123.9(CH_{Ar}), 122.6(CH_{Ar}), 121.9(C_{Ar}), 112.3(CH_{Ar}), 53.1(>CH_2), 24.8 (-CH_3, $_{Acetate}$), 21.2 (Ar-CH_3). Anal. calcd (%) for $C_{46}H_{38}N_6O_{10}Pd_2$: C 54.40; H 3.77; N 8.27 Found: C 54.37; H 3.41; N 8.00; FT-IR (KBr, cm^{-1}) 1619 (C=N), 1605, 1576, 1576. HRMS *m/z* calcd. for $C_{46}H_{38}N_6O_8Pd_2$ 1014.0821 [M], 957.0692 $[M\text{-}OAc]^+$; found 957.0651$[M\text{-}OAc]^+$.

Bis(μ-acetato)bis(1-*p*-nitrophenylimino-2-*p*-methoxyphenylisoindoline)dipalladium(II) (7).

Complex **7** was obtained as a yellow powder in 28% yield (207 mg) from **3** (254 mg, 0.707 mmol) and $Pd(OAc)_2$ (190 mg, 0.846 mmol). ^1H NMR ($CDCl_3$): δ 8.09 (d, *J* = 8.0, 2H, Ar), 7.69 (d, *J* = 7.7, 2H, Ar), 7.52 (m, 2H, Ar), 7.32 (d, *J* = 7.5, 2H, Ar), 7.17 (m, 2H, Ar), 7.10 (m, 4H, Ar), 6.62 (d, *J* = 8.7, 2H, Ar), 6.21 (d, *J* = 8.8, 2H, Ar), 5.91 (d, *J* = 8.5, 2H, Ar), 5.83 (d, *J* = 8.2, 2H, Ar), 4.61(d, *J* = 17.2, 2H, C*H*$_2$), 3.22 (s, 6H, Ar-OCH_3), 3.22 (d, *J* = 17.2, 2H, C*H*$_2$), 1.69 (s, 6H, acetate); $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 180.0($C_{acetate}$), 154.6($C_{C=N}$), 152.2(C_{Ar}), 151.0(C_{Ar}), 145.7(C_{Ar}), 141.0 (C_{Ar}) 131.6(CH_{Ar}), 130.5(C_{Ar}), 129.1(C_{Ar}), 128.6(CH_{Ar}), 126.4(CH_{Ar}), 125.8(C_{Ar}), 124.0(CH_{Ar}), 122.6(CH_{Ar}), 122.6(CH_{Ar}), 119.3(CH_{Ar}), 113.1(CH_{Ar}), 112.7(CH_{Ar}),

55.8($C_{Ar\text{-}OMe}$), 53.2(>*C*H_2), 24.5($C_{Me,\ Acetate}$). Anal. Calcd. (%) for $C_{46}H_{38}N_6O_{10}Pd_2$: C 52.74; H 3.66; N 8.02. Found: C 51.90; H 3.59; N 7.79; FT-IR (KBr, cm^{-1}) 1612 (C=N), 1602, 1575. HRMS *m/z* calcd. for $C_{46}H_{38}N_6O_{10}Pd_2$ 1046.0719 [M], 989.0590 $[M\text{-}OAc]^+$; found 989.0615 $[M\text{-}OAc]^+$.

Bis(μ-acetato)bis(1-*p*-nitrophenylimino-2-*p*-isopropylphenylisoindoline)dipalladium(II) (8). Complex **8** was obtained as a yellow powder in 29% yield (212 mg) from **4** (254 mg, 0.684 mmol) and $Pd(OAc)_2$ (184 mg, 0.821 mmol). ^1H NMR ($CDCl_3$): δ 8.05 (d, *J* = 8.6, 2H, Ar), 7.62 (d, *J* = 8.8, 2H, Ar), 7.53(m, 2H, Ar), 7.47 (s, 2H, Ar), 7.27 (d, *J* = 7.5, 2H, Ar), 7.11 (m, 2H, Ar), 7.05 (d, *J* = 8.6, 2H, Ar), 6.95 (d, *J* = 8.2, 2H, Ar), 6.22 (d, *J* = 8.2, 2H, Ar), 5.82 (m, 4H, Ar), 4.54 (d, *J* = 17.3, 2H, C*H*$_2$), 2.95 (sept, *J* = 6.9, 2H, C*H*$(CH_3)_2$), 2.90 (d, *J* = 17.3, 2H, C*H*$_2$), 1.73 (s, 6H, acetate), 1.36 (d, *J* = 6.9, 6H, CH(C*H*$_3)_2$), 1.34 (d, *J* = 6.9, 6H, CH(C*H*$_3)_2$); $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 180.1 ($C_{acetate}$), 152.1, ($C_{C=N}$), 151.3 (C_{Ar}), 145.6(C_{Ar}), 143.9(C_{Ar}), 141.2(C_{Ar}), 134.2(CH_{Ar}), 133.8(C_{Ar}), 131.7(CH_{Ar}), 130.4(C_{Ar}), 129.0(CH_{Ar}), 128.6(CH_{Ar}), 127.0(CH_{Ar}), 126.5(CH_{Ar}), 124.7(CH_{Ar}), 124.2(C_{Ar}), 124.0(CH_{Ar}), 122.8(CH_{Ar}), 122.8(CH_{Ar}), 112.3(CH_{Ar}), 52.9(>CH_2), 34.1(*C*H$(CH_3)_2$), 24.8(-CH_3, Acetate), 24.6(CH(*C*$H_3)_2$), 24.5(CH(*C*$H_3)_2$). Anal. Calcd. (%) for $C_{50}H_{46}N_6O_8Pd_2$: C 56.03; H 4.33; N 7.84. Found: C 55.65; H 4.29; N 7.93; FT-IR (KBr, cm^{-1}) 1614 (C=N), 1604, 1575, 1514. HRMS *m/z* calcd. for $C_{50}H_{46}N_6O_8Pd_2$ 1070.1447 [M], 1013.1318 $[M\text{-}OAc]^+$; found 1013.1316 $[M\text{-}OAc]^+$.

X-Ray structure determinations

Data were collected at -90 °C on a Nonius Kappa CCD diffractometer, using the COLLECT program.[31] Cell refinement and data reductions used the programs DENZO and

SCALEPACK.[32] SIR97[33] was used to solve the structures and SHELXL97[34] was used to refine the structures. ORTEP-3 for Windows[35] was used for molecular graphics and PLATON[36] was used to prepare material for publication. H atoms were placed in calculated positions with U_{iso} constrained to be 1.5 times U_{eq} of the carrier atom for methyl protons and 1.2 times U_{eq} of the carrier atom for all other hydrogen atoms.

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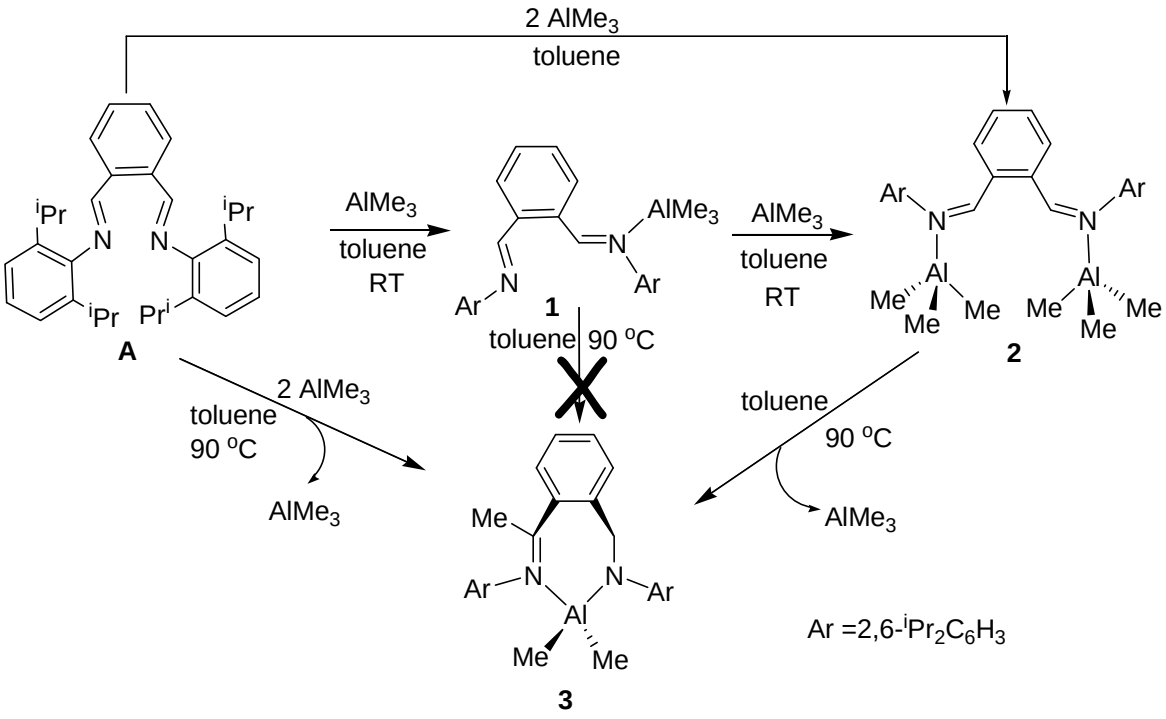
CHAPTER 6

PUBLICATION 5

Description

The following is a manuscript in preparation which describes the synthesis and characterization of a seven-membered, neutral (γ-amidoimino)$AlMe_2$ complex (**3**) obtained from the reaction of γ-diimine with trimethylaluminum (TMA). This chapter also presents other non-chelating γ-diimine aluminum alkyl complexes obtained, which are reaction intermediates in the formation of **3**. By varying reaction conditions, reaction intermediates in the formation of **3** can be isolated and characterized. All compounds (**1-3**) were synthesized and characterized by standard methods, and molecular structures of **2** and **3** were determined by single crystal X-ray analysis.



Authors' Contribution

I synthesized and fully characterized all γ-diimine and γ-amidoimino aluminum alkyl complexes (**1-3**). Dr. Gabriele Schatte did all structural determinations by single crystal X-ray analysis and the work was supervised by Dr. Stephen R. Foley.

Relation of Chapter 6 (Publication 5) to the Overall Objectives of this Project

Consistent with the overall objective of utilizing γ-diimine ligands to synthesize seven-membered coordination complexes (as discussed in Chapter 2) and also motivated by the work that was conducted by our group and others on the reaction of α-diimines with trimethylaluminum to obtain an (α-amidoimino)$AlMe_2$ complex. We therefore investigated the reaction of the γ-diimine ligand (from Chapter 2) with TMA, with the intention of using the resultant complexes in catalytic studies for ε-caprolactone polymerization as mentioned in Chapter 1.8.

6. Synthesis and Characterization of γ-Amidoimino Aluminum Alkyl Complexes from γ-Diimine Ligand

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6.1 Abstract

Depending on the reaction and stoichiometric conditions employed, reaction of trimethylaluminum with the γ-diimine ligand 1,2-(2,6-$^{i}Pr_2C_6H_3N{=}CH)_2$-C_6H_4 results in formation of very different aluminum complexes. Thus, reaction of the γ-diimine with 1 equiv or 2 equiv of $AlMe_3$ (TMA) at ambient temperature gives nonchelating complexes **1** and **2**. On the other hand, when 2 equiv of TMA is used and the reaction heated to 90 ^{o}C for 12 h, formation of neutral seven-membered γ-amidoimino aluminum alkyl complex (**3**) is obtained. Complexes **1** and **2** are shown to be intermediates in the formation of **3**. All complexes were fully characterized by NMR spectroscopy, MS spectrometry, elemental analysis and molecular structures of complexes **2** and **3** were determined by X-ray crystallographic studies.

6.2 Introduction

Coordination chemistry of late transition-metals to α-diimine ligands is well-established.[1] Reports by Brookhart *et al.* regarding the effectiveness of diimine ligands (**A**, Figure 6.1) in supporting late transition metals for α-olefin polymerization has generated much interest in the field of polymer chemistry. These sterically demanding ligands allow control over the molecular weight and microstructure of the resultant polymer.[1-4] Generally, aluminum complexes have been used as active co- and pre-catalysts in polymerization reactions. In particular, aluminum alkoxides have been used as catalysts for the ring-opening polymerization (ROP) of cyclic esters; the resultant polymers are biodegradable and have promising practical applications as surgical sutures and environmentally friendly carrier bags.[5-7] Nitrogen-based bidentate chelating ligands have been sought for many applications due to ease of synthesis, and electronic and steric tunability around the metal centre which is achieved through varying substituents on the nitrogen atoms of the ligand.[1-4] Consequently, chelating nitrogen-based ligands such as neutral α-diimine (**A**),[8-11] monoanionic β-diketiminate (β-amidoimine) (**B**),[12-21] dianionic diamido (**C**),[22] amidinate (**D**),[23-25] guanidinate (**E**) and aminotroponiminate (**F**)[26] ligands (Figure 6.1) have been investigated in alkyl aluminum chemistry as precatalysts for transition-metal free olefin polymerization.

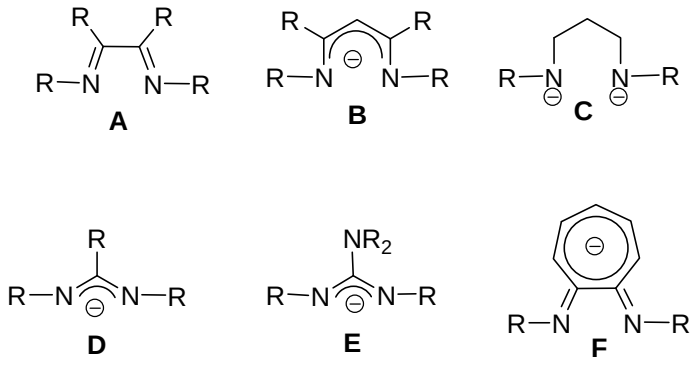
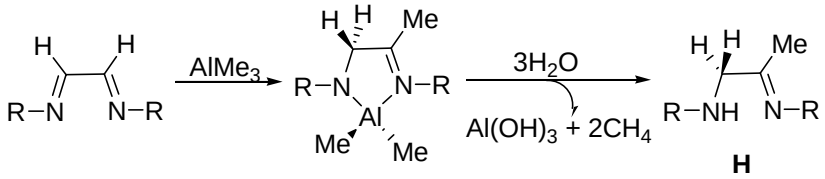


Figure 6.1. Examples of chelating nitrogen-based ligands

Klerks *et al*. reported the reaction of α-diimine ligands with trimethylaluminum to obtain (α-amidoimino)$AlMe_2$ complexes (**G_1-G_3**) as shown in Scheme 6.1.[11] These complexes were presumably formed by aluminum coordination followed by alkylation of the C=N double bond and subsequent intramolecular hydrogen transfer to the other imine double bond resulting in α-amidoimino ligand where the methyl group resides exclusively on the imido carbon of the ligand.



G_1: R = Me_3C

G_2: R = 2,6-Me_2-C_6H_3

G_3: R = 2,4,6-Me_3-C_6H_2

Scheme 6.1. Synthesis and hydrolysis of (α-amidoimino)$AlMe_2$ complexes

Similar α-amidoimine complexes have been reported by Gibson *et al*.(**I**) and Olson *et al.* (**J**) on other ligands with variations in R-groups and in the ligand backbone (Figure 6.2).[9, 27-29] α-Aminoimines (**H**) have also been proposed as ligands in early transition metal chemistry, but have never been actually investigated.[11] One promising and convenient general synthesis of such ligands is by controlled hydrolysis of aluminum alkyl complexes (Scheme 6.1).[11] This technique has been used in the literature for formation of a pyridine amidoimino ligand as shown in complex **K**.[30, 31]

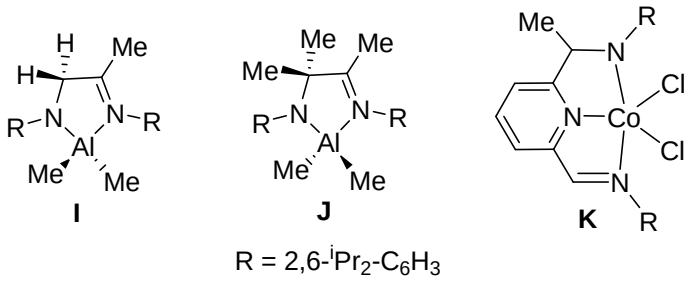
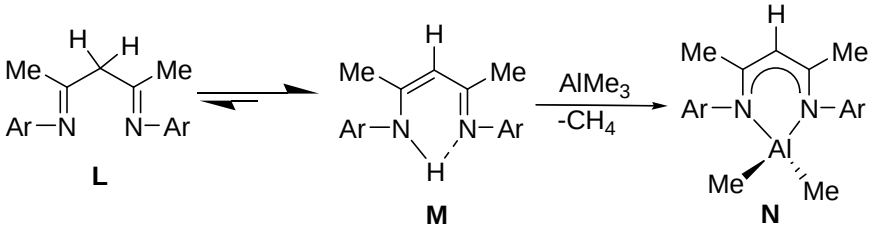


Figure 6.2. Examples of (α-amidoimino)$AlMe_2$ (**I** and **J**) and pyridine amidoimino-based Co(III) complex (**K**)

β-diimine ligands (**L**) with a CH_2 group in their backbones readily tautomerize to their enamine isomer (**M**). When **M** is reacted with aluminum alkyls, deprotonation of the ligand occurs and this produces the corresponding β-diketiminato aluminum alkyl complex **N**.[12-21]



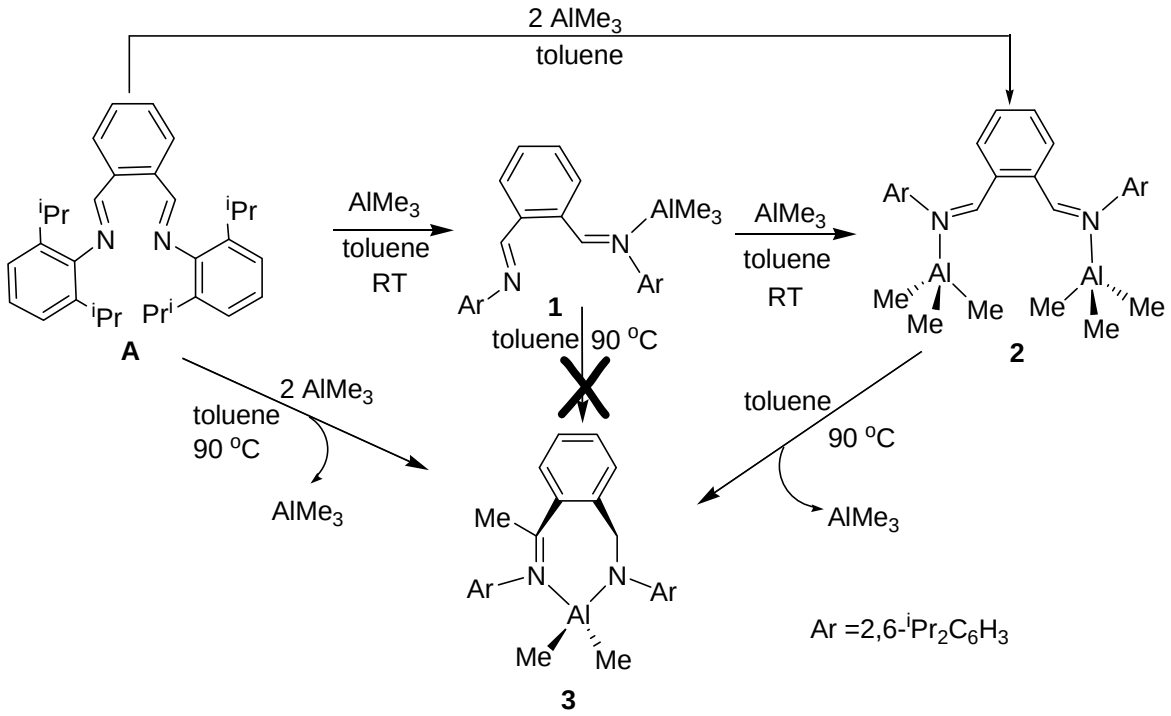
Scheme 6.2. Reaction of β-diimine (**L**) (β-diketimine (**M**)) ligands with aluminum alkyls

To the best of our knowledge, reports on the reaction of γ-diimine analogous to α-diimine ligands with aluminum alkyls do not exist in the literature. Herein, we report on the synthesis and characterization of a new neutral aluminum complex carrying a bidentate monoanionic γ-amidoimino ligand.

6.3 Results and discussion

Depending on the reaction and stoichiometric conditions employed, reaction of trimethylaluminum ($AlMe_3$) with the γ-diimine ligand 1,2-(2,6-$^{i}Pr_2C_6H_3N{=}CH)_2$-C_6H_4 (**A**) results in diverse aluminum complexes. Thus, as shown in Scheme 6.3, reaction of **A** with equimolar amounts of $AlMe_3$ (TMA) at ambient temperature results in nonchelating complex **1**, in which $AlMe_3$ is coordinated to one imine nitrogen while the other imine nitrogen remains uncoordinated. This is readily observed by ^{1}H NMR spectroscopy (C_6D_6), which showed the two imine (*H*C=N) protons were no longer chemically equivalent, with two characteristic singlets each integrating for one proton appearing downfield at δ 9.87 and upfield at δ 8.07 from that of the free ligand **A**, which (in C_6D_6) shows a distinct singlet at δ 8.88 integrating for two imine (–N=C*H*–) protons. When an additional equiv of TMA was reacted with complex **1**, complex **2** was obtained, wherein the γ-diimine ligand acts as a bidentate, non-chelating ligand bridging the two TMA groups through coordination to the imine moieties. ^{1}H NMR spectroscopy of complex **2** showed chemically equivalent imine protons with the characteristic *H*C=N singlet appearing downfield at δ 9.87, relative to ligand **A**. Complex **2** was also obtained when **A** is reacted directly with 2 equiv of TMA at room temperature. Heating compound **2** at 90 ^{o}C for 12 h transformed the neutral diimine ligated aluminum dinuclear complex into a neutral chelating seven-membered (γ-amidoimino)$AlMe_2$ complex **3**, presumably through alkylation of one imine carbon and followed by intramolecular hydrogen transfer to another imine carbon as proposed by Klerks *et al.* for analogous α-diimine aluminum complexes.[11] The same result is obtained when **A** is directly reacted with 2 equiv of TMA at 90 ºC for 12 h. ^{1}H NMR spectroscopy of **3** shows two doublets at δ 4.8 and 3.7, each corresponding to one proton for amine (–N-CH_2–) functionality, indicating their diastereotopic nature and the formation of a C_1 symmetric species. The methyl group on the

imine carbon (N=CCH_3) appears at δ 1.7. The two methyl groups coordinated to aluminum (Al-CH_3) appear at δ -0.87 and -0.94. These results are consistent with initial formation of **1**, followed by **2** and subsequent migration of the methyl group and then intramolecular hydrogen transfer resulting in (γ-amidoimino)$AlMe_2$ complex (**3**). Interestingly, compound **1** is unreactive in toluene at 90 ^oC and does not result in formation of **3** and only does so if the second equiv of $AlMe_3$ is added. All complexes were fully characterized by NMR spectroscopy, mass spectrometry, elemental analysis and molecular structures of complexes **2** and **3** were determined by X-ray crystallographic studies.



Scheme 6.3. Reaction of γ-diimine ligand **A** with $AlMe_3$ using different reaction conditions

Microanalytical data for all complexes are consistent with the proposed structures (see experimental section). To fully characterize these complexes, molecular structures of **2** and **3**

were determined by X-ray crystallographic analysis. The structures confirm the non-chelating bridging mode in **2**, where each imine group is bound to a separate Al centre, while **3** shows a bidentate chelating monoanionic γ-amidoimino ligand coordinated to aluminum (Figure 6.3 and Figure 6.4). The Al center in both complexes is an expected distorted-tetrahedral geometry. In complex **2**, Al(1)-N(1) and Al(2)-N(2) bond distances are similar, [2.0588(17) and 2.0799(16) Å, respectively], as well as the N(1)-C(13) [1.287(2)] and N(2)-C(20) [1.282(2)] bond distances. These N-C bond distances are consistent with imine double bond character and also unambiguously confirming a C_{2v} symmetric compound. On the contrary, in complex **3** the two Al-N bond distances are different. The Al-N_{imino} bond distance [Al(1)-N(1), 2.0524(15) Å] is significantly longer than the Al-N_{amido} bond distance [Al(1)-N(2), 1.8541(14) Å]. The presence of distinct imino C=N and amido C-N functionalities in **3** was confirmed by the difference in their C-N bond distances. The imine bond [N(2)-C(20), 1.471(2)] was shorter than the amide bond [N(1)-C(13), 1.294(2)] by 0.17 Å. The Al-N_{imino} bond distance 2.0524(15) Å and is in the normal range for Al-N dative bonds [1.957(3)-2.238(4)].[9, 27-29]

The bite angle N(1)-Al-N(2) for complex **3** is 100.24(6)º, and shows the largest angle compared with analogous (α-amidoimino)$AlMe_2$ (84.5(1)º)[9] and (β-diketiminato)$AlMe_2$ (94.72(14)º)[21] complexes. The five- and six-membered rings formed from α- and β-diimines, respectively, are essentially planar, while in the seven-membered ring from complex **3** the aryl group is tilted out of the N(1)-Al(1)-N(2) plane (α = 89.91º) and is the reason why C_1 symmetry was observed by NMR (Figure 6.5). Thus, interconversion of the puckered seven-membered ring system is slow on an NMR time scale. ORTEP plots of **2** and **3** are shown in Figures 6.3 and 6.4 with bond distances and angles indicated in their respective captions. Crystallographic data and refinement parameters are summarized in Table 6.1.

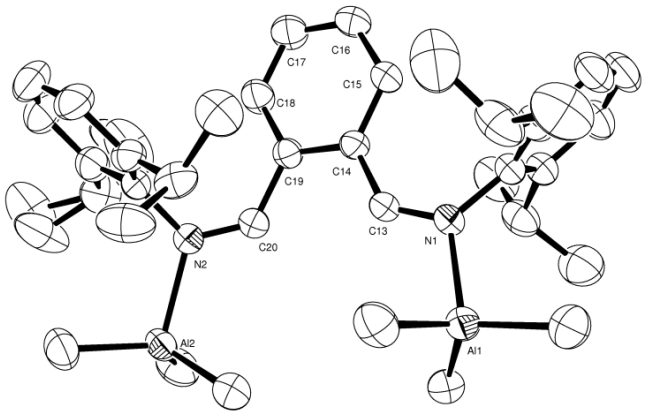


Figure 6.3. ORTEP plot of **2** at the 50% probability level. The hydrogen atoms have been omitted for clarity. Selected bond lengths [Å] and angles [^{o}]: Al(1)-N(1) = 2.0588(17), Al(2)-N(2) = 2.0799(16), Al(1)-C(43) = 1.961(2), Al(1)-C(42) = 1.968(2), Al(1)-C(41) = 1.982(2), Al(2)-C(44) = 1.956(2), Al(2)-C(46) = 1.962(3), Al(2)-C(45) = 1.971(2), N(1)-C(13) = 1.287(2), N(2)-C(20) = 1.282(2), C(43)-Al(1)-N(1) = 106.09(9), C(42)-Al(1)-N(1) = 100.37(9), C(41)-Al(1)-N(1) =101.57(9), C(44)-Al(2)-N(2) = 103.90(9), C(46)-Al(2)-N(2) = 101.11(9), C(45)-Al(2)-N(2) = 105.78(9).

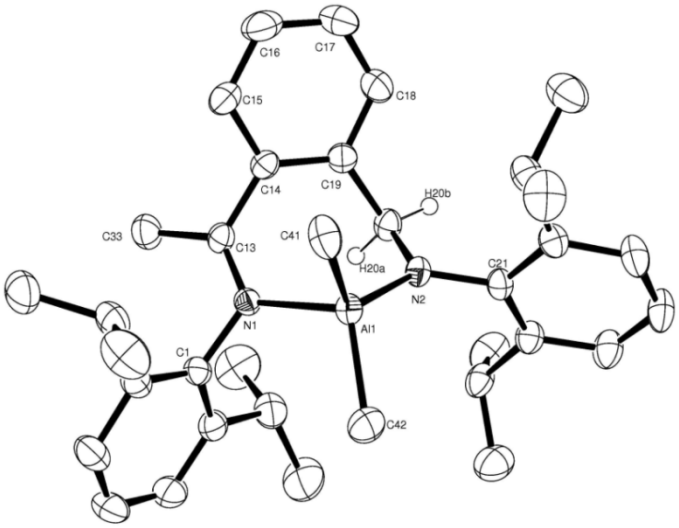


Figure 6.4. ORTEP plot of **3** at the 50% probability level. The hydrogen atoms have been omitted for clarity. Selected bond lengths [Å] and angles [^{o}]: Al(1)-N(2) = 1.8541(14), Al(1)-C(42) =

1.966(2), Al(1)-C(41) = 1.982(2), Al(1)-N(1) = 2.0524(15), N(1)-C(13) = 1.294(2), N(1)-C(1) = 1.467(2), N(2)-C(21) = 1.434(2), N(2)-C(20) = 1.471(2), N(2)-Al(1)-C(42) = 111.86(8), N(2)-Al(1)-C(41) = 117.62(8), C(42)-Al(1)-C(41) = 116.14(9), N(2)-Al(1)-N(1) = 100.24(6), C(42)-Al(1)-N(1) = 106.25(8), C(41)-Al(1)-N(1) = 102.08(7), C(13)-N(1)-Al(1) = 123.55(12), C(1)-N(1)-Al(1) = 116.64(11), C(21)-N(2)-Al(1) = 125.92(11), C(20)-N(2)-Al(1) = 118.88(10)

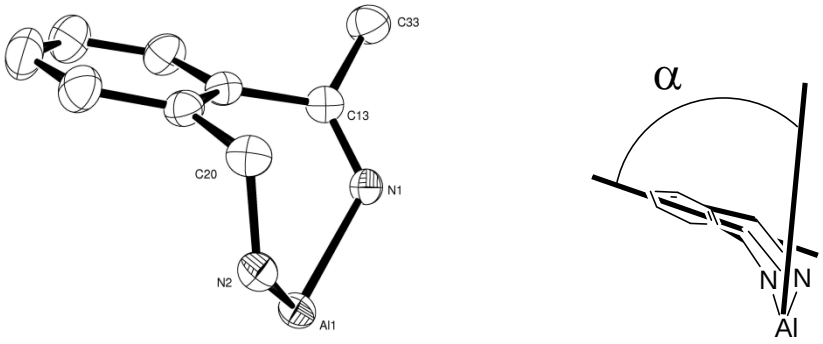


Figure 6.5. Seven-membered ring from γ-(amidoimino)$AlMe_2$ complex **3**. A ChemDraw drawing of **3** shows the α-angle, which is the angle between the C_6H_4 and N(2)-Al(1)-N(1) planes. Methyl groups on aluminum and $^{i}Pr_2C_6H_3$ groups on N atoms have been removed for clarity.

Table 6.1. Crystal data and refinement parameters for complexes **2** and **3**.

	2	**3**
formula	$C_{38}H_{58}Al_2N_2$	$C_{35}H_{49}Al_1N_2$
formula wt	596.82	524.74
Color/Habit	yellow, rod	orange, block
crystal system	monoclinic	monoclinic
space group	$P2_1/c$	$P2_1/c$
a, Å	9.3174(2)	16.971(4)
b, Å	20.1836(5)	10.8665(4)
c, Å	22.0120(4)	18.5696(6)
α, (^{o})	90	90
β, (^{o})	91.3617(13)	113.1331(14)
γ, (^{o})	90	90
Z	4	4
ρ_{calc}, Mg m^{-3}	1.023	1.107
temp, K	183(2)	183(2)
F(000)	1304	1144
reflns collected	14032	22123
Independent reflns	7311	6429
R_{int}	0.0331	0.0646
θ range, deg	3.19 to 25.38	2.22 to 26.371
final R_1(I >2σI)	R_1 = 0.0486, wR_2 = 0.1133	R_1 = 0.0480, wR_2 = 0.1224

6.4 Conclusion

Depending on reaction conditions and stoichiometry employed, different complexes are obtained when $AlMe_3$ is reacted with the γ-diimine ligand 1,2-(2,6-$^{i}Pr_2C_6H_3N{=}CH)_2$-C_6H_4. Thus, reaction of the γ-diimine with 2 equiv of $AlMe_3$ in toluene at 90 ºC results in formation of neutral seven-membered (γ-amidoimino)$AlMe_2$ complex **3**, presumably through aluminum coordination, then methyl transfer to an imine carbon followed by hydrogen migration from the imine carbon. On the other hand, reaction of **A** with equimolar amounts or 2 equiv of $AlMe_3$ at room temperature result in complex **1** and **2**, respectively. Complex **1** and **2** are proposed intermediates in the formation of **3**. Application of **3** for the polymerization of ε-caprolactone as well as its hydrolysis and subsequent coordination of the resultant ligand to early transition metals for use in ethlyene polymerization are currently being examined in our laboratory and these results will be reported at a later date.

6.5 Experimental Section

General Information. Unless otherwise stated, all reactions were performed under N_2 using standard Schlenk techniques or in a N_2-filled drybox. Solvents were dried using an MBraun solvent purification system and stored under nitrogen. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker 500 MHz Avance spectrometer. Chemical shifts for ^{1}H and ^{13}C NMR are reported in ppm in reference to the residual ^{1}H and ^{13}C resonances of C_6D_6 (^{1}H: δ 7.16; ^{13}C: δ 128.39). Coupling constants are given in Hz. Elemental analyses were performed on a Perkin-Elmer 2400 CHN elemental analyzer. Mass spectral data were obtained using Applied Biosystem QSTAR®XL MS/MS System (ESI-Q-TOF) and VG70 SE (Double Focusing EI). Trimethylaluminum (TMA, 2M solution in toluene) and 2,6-diisopropylaniline were purchased

from Sigma-Aldrich Chemical Company and phthalaldehyde was purchased from Alfa Aesar and all compounds were used as received. The γ-diimine ligand, 1,2-(2,6-$^{i}Pr_2C_6H_3N{=}CH)_2$-C_6H_4, **A**, was synthesised as previuosly reported.[32]

Synthesis of non-chelating [1,2-(2,6-$^{i}Pr_2C_6H_3N{=}CH)_2$-C_6H_4]$AlMe_3$ complex (1)

A flask was charged with γ-diimine (300.0 mg, 0.663 mmol) and $AlMe_3$ (0.332 mL, 2.0 M, 0.663 mmol) in toluene (20 mL) to form a yellow homogeneous solution. After 12 h of stirring at ambient temperature under dinitrogen, the reaction mixture was concentrated to 5 mL, then 1 mL of hexanes was added and the mixture was cooled to -30 ºC, where yellow crystals of **1** suitable for X-ray diffraction studies were obtained (244 mg, 70%). Repeating the reaction at 90ºC did not affect the reaction outcome. ^{1}H NMR (C_6D_6): δ 9.87 (s, 1H, N=C*H*), 8.07 (s, 1H, N=C*H*), 7.19-7.05 (m, 6H, Ar), 6.98 (d, *J* = 7.6, 1H, C_6H_4), 6.98 (d, *J* = 8.0, 1H, C_6H_4), 6.75 (m, 1H, C_6H_4), 6.45 (m, 1H, C_6H_4), 3.32 (sept., *J* = 6.8, 2H, C*H*$(CH_3)_2$), 3.10 (sept., 2H, *J* = 6.8, C*H*$(CH_3)_2$), 1.33 (d, *J* = 6.8, 6H, CH(C*H*$_3)_2$), 1.27 (d, *J* = 6.8, 12H, CH(C*H*$_3)_2$), 0.82 (d, *J* = 6.8, 6H, CH(C*H*$_3)_2$), -0.35 (s, 9H, $AlMe_3$). $^{13}C\{^{1}H\}$ NMR (C_6D_6): δ 169.6 ($C_{C=N}$), 161.6($C_{C=N}$), 149.2(C_{Ar}), 140.6(C_{Ar}), 140.1(C_{Ar}), 137.7(C_{Ar}) 137.3(C_{Ar}), 133.1(C_{Ar}), 132.0(CH_{Ar}), 130.6(CH_{Ar}), 129.9(CH_{Ar}), 129.6(CH_{Ar}), 128.5(CH_{Ar}), 125.7(CH_{Ar}), 124.7(CH_{Ar}), 123.5(CH_{Ar}), 28.6(*C*H$(CH_3)_2$), 28.4(*C*H$(CH_3)_2$), 28.4(CH(*C*H$_3)_2$), 24.5(CH(*C*H$_3)_2$), 24.1(CH(*C*H$_3)_2$), 23.6(CH(*C*H$_3)_2$), 23.5(CH$(CH_3)_2$), -7.5 ($AlMe_3$). Anal. Calcd. for $C_{35}H_{49}AlN_2$: C 80.11; H 9.41; N 5.34. Found: C 79.90; H 9.93; N 5.24.

Synthesis of non-chelating [1,2-(2,6-$^{i}Pr_2C_6H_3N{=}CH)_2$-C_6H_4]$(AlMe_3)_2$ complex (2)

Method 1 (Direct reaction from **A** to **2**): A reaction tube was charged with γ-diimine (300 mg, 0.663 mmol) and $AlMe_3$ (0.663 ml, 2.0 M, 1.326 mmol) in toluene (20 mL) to form a yellow homogeneous solution, which was stirred at ambient temperature under dinitrogen. After 12 h the mixture was concentrated to 5 mL, then 1 mL of hexanes was added and the mixture was cooled to -30 ºC, where yellow crystals of **2** suitable for X-ray diffraction studies were obtained (264 mg, 67%).

Method 2 (Formation of **2** from **1**): A reaction tube was charged with **1** (20 mg, 0.0381 mmol) and $AlMe_3$ (0.020 mL, 0.0400 mmol) in toluene (5 mL). The mixture was stirred at room temperature for 12 h. ^{1}H NMR was taken and showed formation of **2** in quantitative yield. ^{1}H NMR (C_6D_6): δ 9.87 (s, 2H, N=C*H*), 7.16-7.10 (m, 6H, C_6H_3), 6.96 (m, 2H, C_6H_4), 6.18 (m, 2H, C_6H_4), 3.35 (m, 4H), 0.93 (d, J = 6.8, 12H, CH(CH_3)$_2$), 0.89 (d, J = 6.8, 12H, CH(CH_3)$_2$), -0.05 (s, 18H, $AlMe_3$). $^{13}C\{^{1}H\}$ NMR (C_6D_6): δ 166.0 ($C_{C=N}$), 149.2(C_{Ar}), 140.6(C_{Ar}), 140.1(C_{Ar}), 137.7(C_{Ar}) 137.3(C_{Ar}), 133.1(C_{Ar}), 132.0(CH_{Ar}), 130.6(CH_{Ar}), 129.9(CH_{Ar}), 129.6(CH_{Ar}), 128.5(CH_{Ar}), 125.7(CH_{Ar}), 124.7(CH_{Ar}), 123.5(CH_{Ar}), 28.6($CH(CH_3)_2$), 28.4($CH(CH_3)_2$), - 6.6 ($AlMe_3$). Anal. Calcd for $C_{38}H_{58}Al_2N_2$: C 76.47; H 9.79; N 4.69. Found: C 76.61; H 9.51 N 4.95.

Synthesis of chelating (γ-amidoimino)$AlMe_2$ complex (3).

Method 1 (Direct reaction from **A** to **3**): A reaction tube was charged with γ-diimine (300 mg, 0.663 mmol) in toluene (30 mL) and $AlMe_3$ (0.762 mL, 2.0 mol/L, 1.52 mmol) was added. The tube was sealed and placed in a preheated sand bath (90 ^{o}C) and stirred for 12 h. Upon cooling, the solvent was concentrated to about 2 mL, then hexanes was added to form a suspension. The suspension was filtered and washed with hexanes (3x10 mL), and then dried

under vacuum to obtain an orange solid of **3** (340.8 mg, 98%). Single X-ray quality crystals were obtained from a hexanes:toluene (1:1) mixture at -30 ^{o}C.

Method 2 (Formation of **3** from **2**): A reaction tube was charged with **2** (10 mg) in toluene (5 mL). The tube was sealed and placed on a preheated sand bath (90 ^{o}C) and stirred for 12 h. Upon cooling, toluene was evaporated and ^{1}H NMR showed quantitative formation of **3**. ^{1}H NMR (C_6D_6): δ 6.97-7.25 (m, 10H, Ar), 4.84 (d, *J* = 10.8, 1H, N-C*H*$_2$), 3.93 (br, 1H, C*H*(CH$_3$)$_2$), 3.76 (m, 1H, C*H*(CH$_3$)$_2$), 3.76 (m, 1H, N-C*H*$_2$), 3.65 (br, 1H, C*H*(CH$_3$)$_2$), 2.98 (br, 1H, C*H*(CH$_3$)$_2$), 1.67 (s, 3H, N=C(C*H*$_3$), 1.56 (br, 3H, CH(C*H*$_3$)$_2$), 1.48 (br, 3H, CH(C*H*$_3$)$_2$), 1.44 (br, 3H, CH(C*H*$_3$)$_2$), 1.35 (br, 3H, CH(C*H*$_3$)$_2$), 1.27 (br, 3H, CH(C*H*$_3$)$_2$), 1.21 (br, 3H, CH(C*H*$_3$)$_2$), 1.07 (br, 3H, CH(C*H*$_3$)$_2$), 1.03 (br, 3H, CH(C*H*$_3$)$_2$), -0.87 (s, 3H, AlMe), -0.94 (s, 3H, AlMe). ^{13}C{^{1}H} NMR (C_6D_6): δ 186.7 ($C_{C=N}$), 152.3(C_{Ar}), 148.3(C_{Ar}), 148.0(C_{Ar}), 142.9(C_{Ar}), 141.5(C_{Ar}), 140.2(C_{Ar}), 136.7(C_{Ar}), 132.2(CH_{Ar}), 131.9(CH_{Ar}), 128.9(C_{Ar}), 128.7(C_{Ar}), 128.5(CH_{Ar}), 126.9(CH_{Ar}), 125.7(CH_{Ar}), 124.9(CH_{Ar}), 124.7(CH_{Ar}), 124.4(CH_{Ar}), 124.3(CH_{Ar}), 61.0(–N–*C*H$_2$–), 30.6(CH(CH$_3$)$_2$), 29.4(CH(CH$_3$)$_2$), 29.2(CH(CH$_3$)$_2$), 28.2(CH(CH$_3$)$_2$), 27.7(CH(CH$_3$)$_2$), 27.2(CH(CH$_3$)$_2$), 26.5(–N=C(*C*H$_3$), 26.4(CH(CH$_3$)$_2$), 26.1(CH(CH$_3$)$_2$), 25.9(CH(CH$_3$)$_2$), 25.6(CH(CH$_3$)$_2$), 24.8(CH(CH$_3$)$_2$), 24.3(CH(CH$_3$)$_2$), -5.38 (AlMe), -9.74 (AlMe). Anal. Calcd. for $C_{35}H_{49}AlN_2$: C 80.11; H 9.41; N 5.34. Found: C 80.10; H 9.35 N 5.31.

6.6 X-ray structure determinations

Data were collected at -90 °C on a Nonius Kappa CCD diffractometer, using the COLLECT program.[33] Cell refinement and data reductions used the programs DENZO and SCALEPACK.[34] SIR97[35] was used to solve the structures and SHELXL97[36] was used to refine

the structures. ORTEP-3 for Windows[37] was used for molecular graphics and PLATON[38] was used to prepare material for publication. H atoms were placed in calculated positions with U_{iso} constrained to be 1.5 times U_{eq} of the carrier atom for methyl protons and 1.2 times U_{eq} of the carrier atom for all other hydrogen atoms.

6.7 Acknowledgments

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6.8 References

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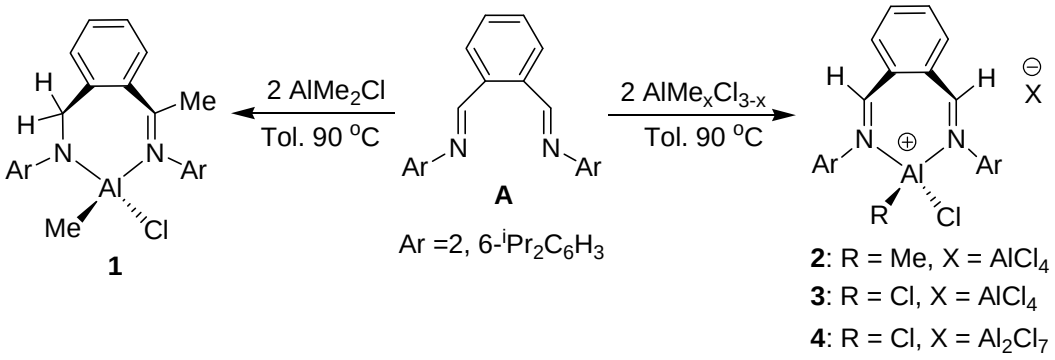
CHAPTER 7

PUBLICATION 6

Description

The following is a manuscript in preparation which describes the synthesis and characterization of a series of seven-membered neutral (**1**) and cationic aluminum alkyl and halide complexes (**2-4**). (γ-amidoimino)Al(Me)Cl (**1**) was obtained by reaction of γ-diimine (**A**) with 2 equiv $AlMe_2Cl$, while reaction of **A** with 2 equiv of $AlMeCl_2$ instead resulted in a monocationic aluminum complex, $[(\gamma\text{-diimine})AlMeCl]^+[AlCl_4]^-$ (**2**) with chelating γ-diimine ligand. Treating **A** with 2 equiv of $AlCl_3$ gave cationic aluminum halide complex $[(\gamma\text{-diimine})AlCl_2]^+[AlCl_4]^-$ (**3**). It was also observed that addition of 3 equiv of $AlCl_3$ gave complex **4**, which shows the same cation as **3**, but $[Al_2Cl_7]^-$ becomes the counter ion.



Authors' Contribution

I synthesized and fully characterized all the γ-diimine based aluminum coordination complexes (**1-4**). Dr. Gabriele Schatte did all the structural determinations by single crystal X-ray

analysis and the work was supervised by Dr. Stephen R. Foley. Written permission was obtained from all contributing authors to include the material within this thesis.

Relation of chapter 7 (Publication 6) to the overall objectives of this project

This is a continuation of the work that was reported in chapters 2 and 6 in that the formation of seven-membered aluminum complexes were obtained by reacting a γ-diimine ligand with a variety of aluminum precursors. However, in this Chapter, we did not only obtain a neutral (γ-amidoimino)$AlMe_2$ complex, but also cationic aluminum complexes containing a chelating γ-diimine ligand. This is the first time we have observed the γ-diimine ligand coordinating in a chelating neutral fashion. Due to increased Lewis acidity of the Al center, cationic aluminum complexes can be more advantageous for catalysis than their analogous neutral aluminum complexes in the ring-opening polymerization of lactones and lactides, for example.

7. Cationic and Neutral Aluminum Complexes based on a γ-Diimine Ligand

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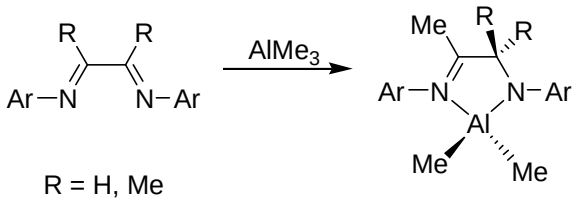
7.1 Abstract

Depending on the aluminum species (Me_2AlCl, $MeAlCl_2$, $AlCl_3$) and reaction conditions employed, different complexes are obtained when these aluminum reagents are reacted with the γ-diimine ligand 1,2-(2,6-$^{i}Pr_2C_6H_3N{=}CH)_2$-C_6H_4. Reaction of a γ-diimine with 2 equiv of Me_2AlCl in toluene results in formation of a neutral seven-membered (γ-amidoimino)Al(Me)Cl (**1**) complex through methyl transfer and subsequent hydrogen migration on the imine carbon. On the other hand, reaction of **A** with 2 equiv of $AlMeCl_2$ resulted in a monocationic aluminum complex, $[(\gamma\text{-diimine})AlMeCl]^+[AlCl_4]^-$ (**2**) with a neutral chelating γ-diimine ligand. Treating **A** with 2 equiv of $AlCl_3$ gave a cationic aluminum halide complex, $[(\gamma\text{-diimine})AlCl_2]^+[AlCl_4]^-$ (**3**). In addition, using 3 equiv of $AlCl_3$ gave complex **4**, which has the same cation as **3**, but contains $[Al_2Cl_7]^-$ as the counter ion. Complexes were characterized by NMR spectroscopy, mass spectrometry, elemental analysis and molecular structures of complexes **1**-**4** were determined by X-ray crystallographic studies.

7.2 Introduction

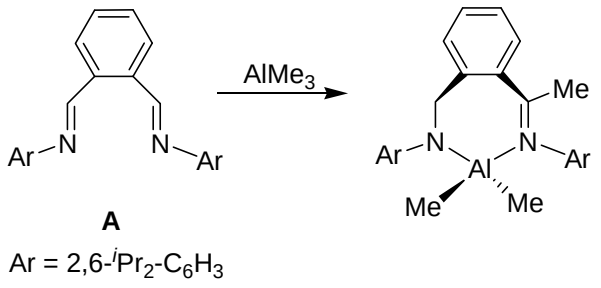
Aluminum compounds have found extensive use in the polymer industry as co-catalysts or precatalysts in olefin polymerization and ring-opening polymerization (ROP) of lactides, lactones and epoxides.[1-8] Due to increased Lewis acidity at the Al center, cationic aluminum complexes are more desired for catalysis than their analogous neutral aluminum complexes for such applications.[9] Common ligands that have been explored in aluminum coordination chemistry include chelating nitrogen-based ligands such as those made popular after the report by Brookhart *et al*. regarding the effectiveness of α-diimine ligands in supporting late transition metals for olefin polymerization.[10-12] Consequently, a wide variety of sterically demanding and chelating ligands such as neutral diimine-, monoanionic β-diketiminato- and dianionic diamido-based ligands have been synthesized. The advantage with these ligands is the ease with which steric and electronic control around the metal centre is introduced by simply changing the substituents on the nitrogen atoms of the ligand.[11, 13] From our previous work, as well as work by others, reaction of α- and γ-diimines with $AlMe_3$ afforded the corresponding (amidoimino)$AlMe_2$ species as shown in Schemes 7.1 and 7.2.[14-16]



R = H, Me

Ar = 2,6-$^{i}Pr_2$-C_6H_3

Scheme 7.1. Reaction of α-diimine with $AlMe_3$[15]



Scheme 7.2. Reaction of γ-diimine (**A**) with $AlMe_3$[17]

Additionally, reaction of **A** with $(CH_3CN)_2PdCl_2$ afforded non-chelating dinuclear palladium chloride complex (**B**), while with $Pd(OAc)_2$, an S-shaped trinuclear palladacycle (**C**) was obtained as shown in Figure 7.1. Under reaction conditions employed, none of these reactions resulted in chelating neutral seven-membered complexes.[18]

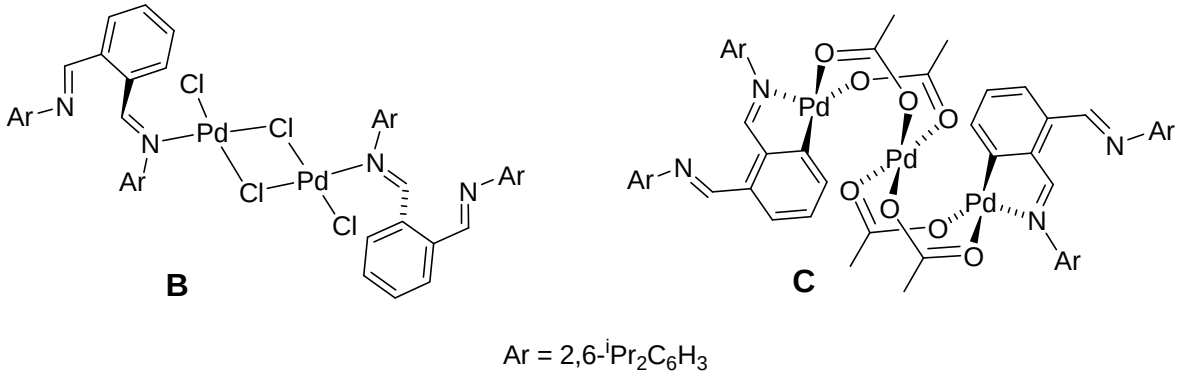


Figure 7.1. Products from the reaction of **A** with $PdCl_2$ and $Pd(OAc)_2$[18]

Therefore, our goal was to investigate the potential of γ-diimines to behave as neutral chelating ligands similar to the popular α-diimine analogues. Consequently, we reasoned that to prevent alkylation of an imine moiety in **A**, reaction of **A** with aluminum halides could generate neutral, seven-membered γ-diimine aluminum complexes instead of monoanionic γ-amidoimino

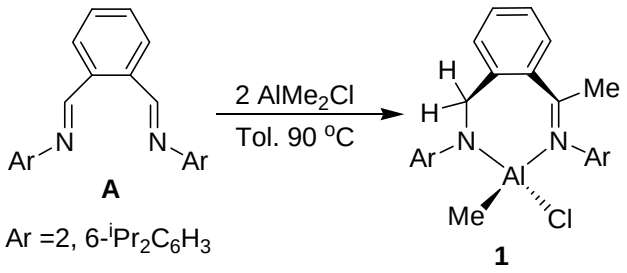
ligands, provided a second equiv of aluminum is used as Lewis acid to generate a cationic Al center.

Herein we report on the syntheses and characterization of neutral and cationic aluminum complexes carrying bidentate monoanionic γ-amidoimino and neutral γ-diimine ligands, respectively. This work represents the first example of definitively characterized complexes exhibiting chelating neutral γ-diimine ligands.

7.3 Results and discussion

Depending on the aluminum species (Me_2AlCl, $MeAlCl_2$, $AlCl_3$) and reaction conditions employed, different complexes are obtained when these aluminum species are reacted with the γ-diimine ligand 1,2-(2,6-$^{i}Pr_2C_6H_3N{=}CH)_2$-C_6H_4. Thus, as shown in Scheme 7.3, reaction of the γ-diimine **A** with 2 equiv of Me_2AlCl in toluene at 90 ºC for 12 h transforms the neutral diimine ligand into a chelating seven-membered monoanionic (γ-amidoimino)AlMeCl complex (**1**). We postulate that the reaction takes place first with aluminum coordination, followed by alkylation of the imine carbon and then intramolecular hydrogen transfer as previously observed before in a reaction of the analogous α-diimines with $AlMe_3$ (Scheme 7.2).[14] The ^{1}H NMR spectrum of ligand **A** in C_6D_6 shows a distinct singlet at δ 8.88 integrating for two chemically equivalent imine (–N=C*H*–) protons. The ^{1}H NMR spectrum of **1** in C_6D_6 shows, among other changes, the absence of any imine (–N=C*H*–) protons between 8-10 ppm and instead the appearance of two doublets at δ 4.8 and 3.7. The coupling constant of these two signals is consistent with diastereotopic methylene protons (–N-CH_2–). The methyl group signal on the imine carbon (N=CCH_3) appears at δ 1.7 and that for methyl group coordinated to aluminum (Al-CH_3) appears at δ - 0.73. These results are consistent with aluminum coordination, methyl migration and then

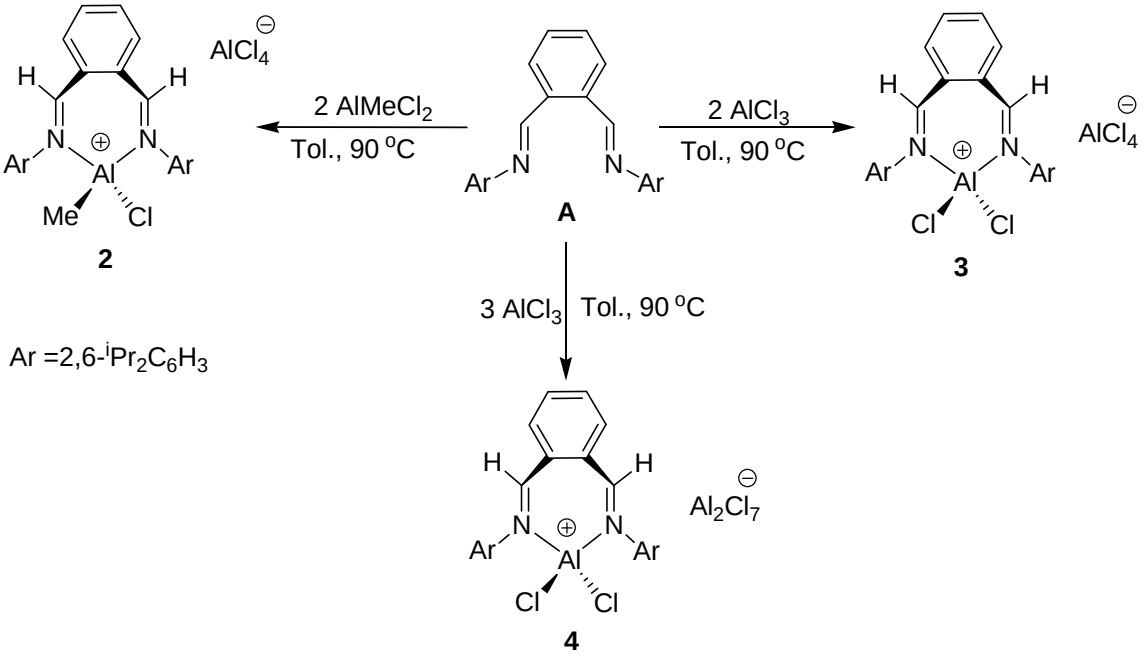
hydrogen transfer resulting in an (γ-amidoimino)Al(Me)Cl complex that is C_1 symmetric, which is consistent with analogous reactions involving α-diimines.[14-17]



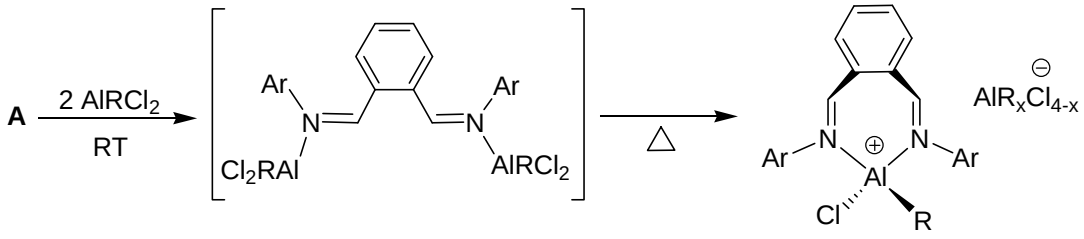
Scheme 7.3. Synthesis of neutral (γ-amidoimino)Al(Me)Cl complex[17]

In contrast to the reaction with Me_2AlCl, treatment of γ-diimine with $MeAlCl_2$ or $AlCl_3$ does not result in a γ-amidoimino aluminum complex but in seven-membered cationic (γ-diimine)AlXCl species, (X = Me(**2**), X = Cl(**3**), (**4**)). Therefore, treatment of **A** with 2 equiv of $MeAlCl_2$ gave a cationic $[(\gamma\text{-diimine})Al(Me)Cl]^+$ complex (**2**) (Scheme 7.4). The chloride and methyl substituents in the counterion appear to be scrambled resulting in the counterion with the general formula $AlMe_xCl_{4-x}$. Of the possible counterions, only the tetrachloroaluminate ($[AlCl_4]^-$) anion was obtained from X-ray diffraction studies. Treating **A** with 2 equiv of $AlCl_3$ gave a cationic aluminum halide complex, $[(\gamma\text{-diimine})AlCl_2]^+[AlCl_4]^-$ (**3**), while using 3 equiv of $AlCl_3$ gave complex **4**, which has the same cation as **3**, but with a heptachlorodialuminate ($[Al_2Cl_7]^-$) counter ion (Scheme 7.4). With regards to complexes **2**-**4** the second equiv of $AlMe_xCl_{3-x}$ (x = 0, 1) is required to abstract a chloride from the first aluminum as shown in Scheme 7.5. This increases the Lewis acidity of the metal centre allowing for the second imine nitrogen to coordinate forming cationic γ-diimine aluminum species having $AlMe_xCl_{4-x}$ as counter ions.

^{1}H NMR for complex **2** shows a characteristic singlet at δ 8.83 integrating for two protons corresponding to the imine (-N=C*H*-) protons and δ - 0.86 for the Al-Me group. In a similar manner, complexes **3** and **4**, whose difference lies only in the counter ion, show a singlet in the ^{1}H NMR spectra each integrating for two imine (-N=C*H*-) protons, and appear at 8.92 and 8.59, respectively.



Scheme 7.4. Synthesis of cationic aluminum complexes



Scheme 7.5. Proposed route into formation of cationic (diimine)Al(R)Cl complexes

Solid-state structures of **1-4** were determined by X-ray crystallographic analysis in order to fully characterize the synthesized compounds. The structures confirm the bidentate chelating monoanionic γ-amidoimino aluminum complex (**1)** and cationic diimine aluminum complexes **2-4** (Figures 7.2-7.5). The Al centers in all the complexes show an expected distorted-tetrahedral geometry. In complex **1**, bond distances between the aluminum and imine nitrogen [Al(1)-N(1) - 2.0524(15) Å] are significantly longer than the amido nitrogen and aluminum bond [Al(1)-N(2) - 1.8541(14) Å]. The presence of $C{=}N_{imino}$ and $C\text{-}N_{amido}$ functionalities were confirmed by their respective C-N bond distances. The N=C imine bond [N(1)-C(13), 1.2294(2)Å] was 0.24 Å longer than the CH_2-N amide bond [N(2)-C(20), 1.471(2)Å]. The Al-N(1) bond distance of 2.0524(15) Å is in the normal range for Al-N dative bonds [1.957(3)-2.238(4)].[19] The imine N=C [N(1)-C(13) and (N(2)-C(20)] bond distances of complexes **2-4** are all within 1.29 ± 0.01 Å and are characteristic of $C(sp^2){=}N$ bond distances, again confirming the diimine nature of ligand **A**. Unlike **1**, both Al(1)-N(1) bond distances in **2, 3** and **4** are similar at 1.94 ± 0.01 Å. These are shorter than the Al-N in **1 [**2.0524(15) Å], consistent with the electrophilic nature of the aluminum centre in complexes **2-4**.

The bite angle N(1)-Al-N(2) for complex **1** is 100.24(6)º, which is significantly smaller than the N(1)-Al-N(2) angle observed in complexes **2** (102.37(13)º), **3** (104.74(7)º) and **4** (102.03(8)º). These angles are larger than those for analogous α-diimine and β-diimine chelating aluminum complexes and are consistent with this larger ring size.[19] Unlike α-diimine and β-diimine aluminum complexes whose five- and six-membered rings are essentially planar, seven-membered rings obtained from the γ-diimine were not planar. The plane of the aryl ring is tilted from the N(1)-Al(1)-N(2) plane by an angle α as shown in Figure 7.6. Complex **1** had an α-angle of 84.97º, while complexes **2-4** gave lower α-angles of 53.29º, 54.26º and 61.06º, respectively.

The larger α-angle in **1** could be due to the presence of amido (H_2C-N) functionality within the ring system. The interconversion of the puckered seven-membered ring system is slow on an NMR time scale and is the reason why C_1 symmetry was observed for complex **1** and C_s symmetry for complexes **2-4** by NMR. The X-ray structure for **1** also showed the Cl(2)/Me(C41) scrambling was occurring resulting in the unit cell of **1** containing 75% of LAl(Me)Cl and 25% of $LAlCl_2$. Their ORTEP plots are shown in Figures 7.2 to 7.5, with bond distances and angles indicated in Table 7.1. Crystallographic data and refinement parameters are summarized in Table 7.2.

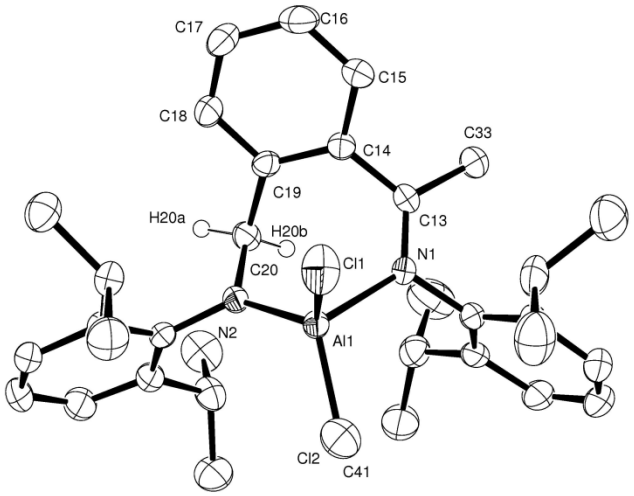


Figure 7.2. ORTEP plot of **1** at the 30% probability level. The hydrogen atoms, with the exception of the amide protons (H20a and H20b), have been omitted for clarity.

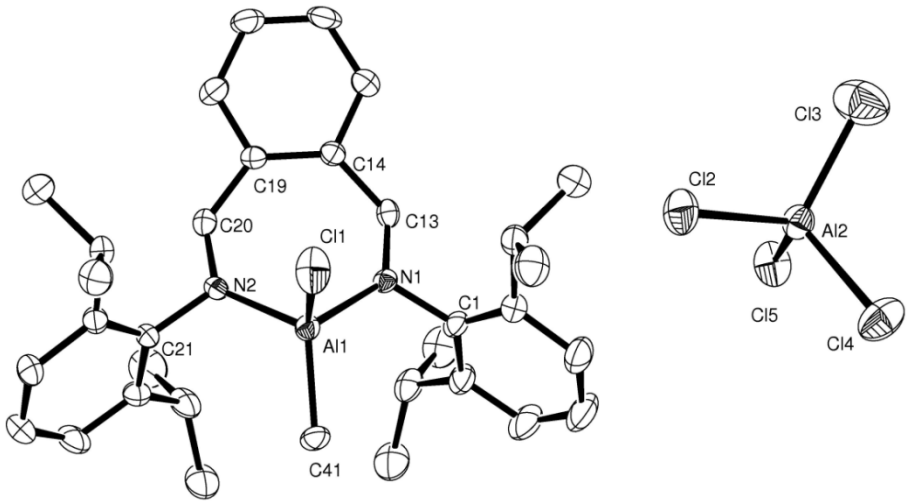


Figure 7.3. ORTEP plot of **2** at the 50% probability level. The hydrogen atoms have been omitted for clarity.

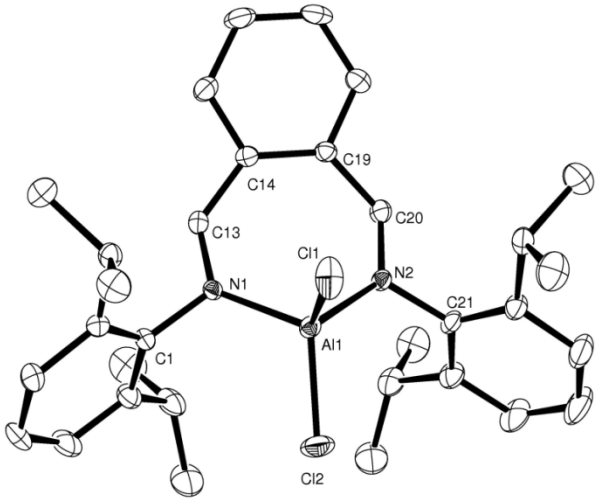


Figure 7.4. ORTEP plot of **3** at the 50% probability level. The hydrogen atoms and counter ion ($[AlCl_4]^-$) have been omitted for clarity.

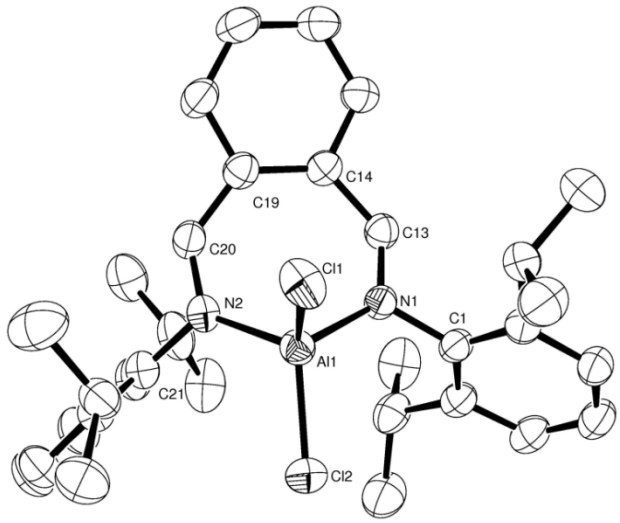
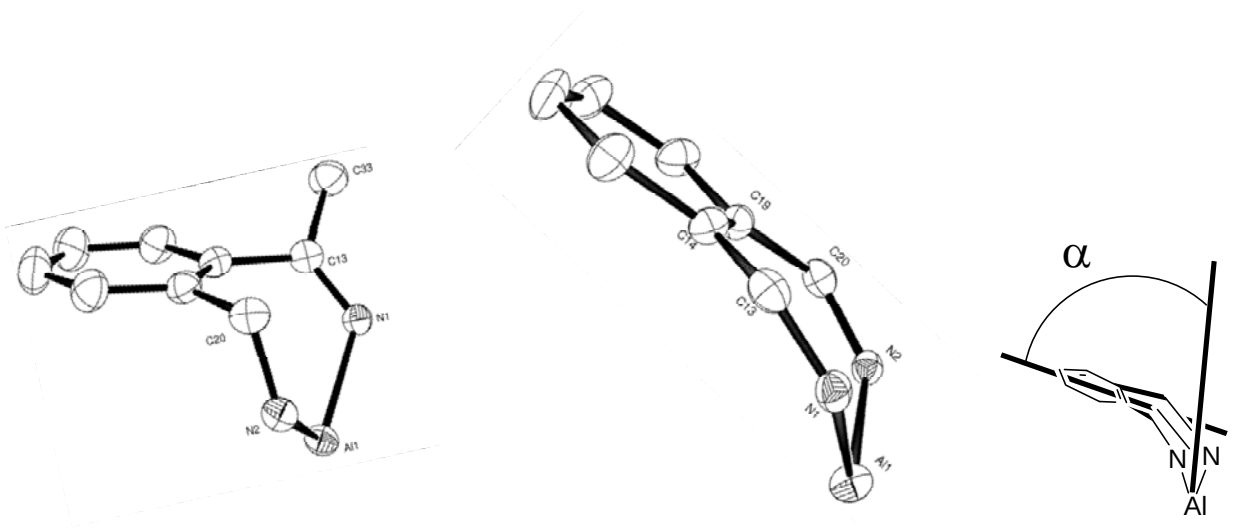


Figure 7.5. ORTEP plot of **4** at the 50% probability level. The hydrogen atoms and counter ion ($[Al_2Cl_7]^-$) have been omitted for clarity.



(**1**) (**4**)

Figure 7.6. Seven-membered ring of (γ-amidoimino)Al(Me)Cl (**1**) and $[(\gamma\text{-diimine})AlCl_2]^+$ (**4**). Me and Cl substituents on aluminum and $^iPr_2C_6H_3$ groups on N atoms have been removed for clarity.

Table 7.1. Selected bond distances (Å) and bond angles (º) of complexes **1, 2·AlCl$_4$, 3·AlCl$_4$** and **4·Al$_2$Cl$_7$**

	1		**2·AlCl$_4$**	**3·AlCl$_4$**	**4·Al$_2$Cl$_7$**
Al(1)-N(1)	2.008(2)	**Al(1)-N(1)**	1.935(3)	1.9243(16)	1.9052(19)
Al(1)-N(2)	1.822(2)	**Al(1)-N(2)**	1.947(3)	1.9170(16)	1.9205(19)
Al(1)-C(41)	1.972(14)	**Al(1)-Cl(1)**	1.935(4)	2.1001(8)	2.0965(9)
Al(1)-Cl(1)	2.1476(12)	**Al(1)-Cl(2)**	2.1047(16)	2.0778(7)	2.0886(9)
N(1)-Cl(2)	2.086(10)	**N(1)-C(13)**	1.287(5)	1.288(2)	1.285(3)
N(1)-C(13)	1.298(4)	**N(2)-C(20)**	1.289(5)	1.288(2)	1.295(3)
N(2)-C(20)	1.471(4)				
N(2)-Al(1)-N(1)	100.24(6)	**N(1)-Al(1)-N(2)**	102.37(13)	104.74(7)	102.03(8)
N(2)-Al(1)-C(42)	111.86(8)	**N(1)-Al(1)-Cl(2)**	110.39(15)	110.70(5)	110.38(6)
N(2)-Al(1)-C(41)	117.62(8)	**N(2)-Al(1)-Cl(2)**	113.00(16)	108.81(5)	110.71(7)
N(1)-Al(1)-C(42)	106.25(8)	**N(1)-Al(1)-Cl(1)**	105.00(10)	106.83(5)	106.03(6)
N(1)-Al(1)-C(41)	102.08(7)	**N(2)-Al(1)-Cl(1)**	119.96(13)	107.07(5)	109.09(6)
C(41)-Al(1)-C(42)	116.14(9)	**Cl(2)-Al(1)-Cl(1)**	104.41(10)	117.86(3)	117.40(4)
C(13)-N(1)-Al(1)	123.55(12)	**C(13)-N(1)-Al(1)**	128.2(2)	126.58(12)	125.33(2)
C(20)-N(2)-Al(1)	118.80(10)	**C(20)-N(2)-Al(1)**	128.4(3)	125.95(13)	122.26(16)
C(1)-N(1)-Al(1)	116.64(11)	**C(1)-N(1)-Al(1)**	113.6(2)	116.44(11)	118.71(13)
C(21)-N(2)-Al(1)	125.92(11)	**C(21)-N(2)-Al(1)**	115.2(2)	115.67(11)	121.55(14)

Table 7.2. Crystal data and refinement parameters for complexes **1, 2·AlCl$_4$, 3·AlCl$_4$** and **4·Al$_2$Cl$_7$**.

	1	**2·AlCl$_4$**	**3·AlCl$_4$**	**4·Al$_2$Cl$_7$**
formula	$C_{33.75}H_{45.25}AlCl_{11.25}N_2$	$C_{33}H_{43}Al_2Cl_5N_2$	$C_{32}H_{40}Al_2Cl_6N_2$	$C_{32}H_{40}Al_3Cl_9N_2$
formula wt	550.26	698.90	719.32	852.65
Color/Habit	yellow, rod	pale yellow, plate	pale yellow, plate	pale yellow, plate
crystal system	monoclinic	triclinic	triclinic	monoclinic
space group	$P2_1/c$	P-1	P-1	$P2_1/c$
a, Å	9.5956(4)	9.4096(4)	9.4550(7)	9.9157(9)
b, Å	15.5935(4)	12.5690(4)	12.4600(4)	13.1391(3)
c, Å	21.5665(8)	16.4848(5)	16.4860(13)	31.8069(8)
α, (°)	90	75.880(3)	75.382(3)	90
β, (°)	102.2337(17)	86.378(2)	86.694(4)	91.1029(11)
γ, (°)	90	73.794(3)	73.725(4)	90
Z	4	2	2	4
ρ_{calc}, Mg m^{-3}	1.159	1.278	1.324	1.367
temp, K	183(2)	183(2)	183(2)	183(2)
F(000)	1184	732	748	1752
reflns collected	10794	10937	13698	25756
Independent reflns	5571	6179	8257	6658
R_{int}	0.0540	0.0517	0.0420	0.0493
θ range, deg	2.33 to 25.03	2.25 to 24.71	2.56 to 27.51	2.78 to 63.86
final R_1(I >2σI)	R_1 = 0.0592, wR_2 = 0.1438	R_1 = 0.0584, wR_2 = 0.1575	R_1 = 0.0387, wR_2 = 0.0872	R_1 = 0.0473, wR_2 = 0.1331

7.4 Conclusion

Our results clearly show that by reducing the degree of alkylation on aluminum precursors, alkylation of the diimine ligand is inhibited favoring formation of a bidentate, chelating coordination mode of the neutral γ-diimine ligand. Accordingly, depending on the aluminum species (Me_2AlCl, $MeAlCl_2$ or $AlCl_3$) and reaction conditions employed, different complexes were obtained when these aluminum species are reacted with the γ-diimine ligand 1,2-(2,6-$^{i}Pr_2C_6H_3N{=}CH)_2$-C_6H_4 (**A**). Thus reaction of **A** with 2 equiv of Me_2AlCl in toluene at 90 ºC results in formation of neutral seven-membered (γ-amidoimino)AlMeCl complex (**1**), presumably through aluminum coordination followed by a methyl transfer and then hydrogen migration from one imine carbon to the resultant amide carbon. On the other hand, reaction of **A** with 2 equiv of $AlMeCl_2$ formed $[(\gamma\text{-diimine})Al(Me)Cl]^+$ complex **2** with a tetrachloroaluminate, $[AlCl_4]^-$ counter ion. Furthermore, a cationic halide complex, $[(\gamma\text{-diimine})AlCl_2]^+$ (**3**) with $[AlCl_4]^-$ was obtained when **A** was treated with 2 equiv of $AlCl_3$. Using 3 equiv of $AlCl_3$, complex **4** was obtained, which has the same cation as **3**, but with heptachlorodialuminate $[Al_2Cl_7]^-$ instead of $[AlCl_4]^-$ as the counter ion. The second equiv of AlR_xCl_{3-x} (x = 0, 1) is required to act as a Lewis acid and abstract a chloride from the first Al, which increases the Lewis acidity of the metal centre allowing for the second imine to coordinate. All complexes were fully characterized by NMR spectroscopy, mass spectrometry, elemental analysis and molecular structures of complexes **1**-**4** were determined by X-ray crystallographic studies. The solution and solid-state data are consistent with a C_1-symmetric structure(**1**), while C_s-symmetry is observed for complexes **2**-**4**.

7.5 Experimental Section

General Information. Unless otherwise stated, all reactions were performed under N_2 using standard Schlenk techniques or in a N_2-filled glovebox. Solvents were dried using an MBraun solvent purification system and stored under nitrogen. ^1H and ^{13}C $\{^1H\}$ NMR spectra were recorded on a Bruker 500 MHz Avance spectrometer. Chemical shifts for ^1H and ^{13}C NMR are reported in ppm in reference to the residual ^1H and ^{13}C resonances of C_6D_6 (^1H: δ 7.16; ^{13}C: δ 128.39). Coupling constants are given in Hz. Elemental analyses were performed on a Perkin-Elmer 2400 CHN elemental analyzer. Mass spectra data were obtained using Applied Biosystem QSTAR®XL MS/MS System (ESI-Q-TOF) and VG70 SE (Double Focusing EI). Reagents such as dimethylaluminum chloride (DMAC, 1 M solution in hexanes), methyl aluminum dichloride (1M solution in Hexanes), aluminum chloride and 2,6-diisopropylaniline were purchased from Sigma-Aldrich Chemical Company, while phthalaldehyde was purchased from Alfa Aesar. All compounds were used as received. The γ-diimine ligand, 1,2-(2,6-^{i}Pr$_2$C$_6$H$_3$N=CH)$_2$-C$_6$H$_4$ (**A**) was synthesized as reported in the literature.[18]

General synthesis for complexes 1-4

Under N_2, a reaction tube was charged with a γ-diimine in toluene (20 mL) and the aluminum species was added. The tube was sealed and placed into a preheated sand bath (90 ^oC) and stirred for 12 h. Upon cooling, the solvent was concentrated to about 2 mL, and then hexanes was added to form a suspension. The suspension was filtered and washed with hexanes, and then dried under vacuum to obtain a pale yellow to yellow solid of **1-4**. Single X-ray quality crystals were obtained from toluene at -30 ºC.

Synthesis of chelating (γ-amidoimino)Al(Me)Cl (1)

A flask was charged with γ-diimine (300.0 mg, 0.663 mmol) and $AlMe_2Cl$ (1.66 mL, 1.0 M, 1.660 mmol) in toluene (20 mL), following the above procedure, to obtain complex **1** as a yellow solid (778.3 mg, 86%). ^{1}H NMR (C_6D_6): δ 7.14-7.37 (m, 10H, Ar), 4.87 (d, *J* = 12.5, 1H, N-C*H*$_2$), 4.11 (sept., *J* = 6.7, 1H, C*H*$(CH_3)_2$), 3.97 (br, 1H, C*H*$(CH_3)_2$), 3.77 (d, *J* = 12.5, 1H, N-C*H*$_2$), 3.62 (br, 1H, C*H*$(CH_3)_2$), 3.54 (br, 1H, C*H*$(CH_3)_2$), 1.78 (s, 3H, N=C(C*H*$_3$), 1.48 (d, *J* = 6.6, 3H, CH(C*H*$_3)_2$), 1.42 (d, *J* = 6.6, 3H, CH(C*H*$_3)_2$), 1.37 (m, 12H, CH(C*H*$_3)_2$), 1.10 (d, *J* = 6.6, 3H, CH(C*H*$_3)_2$), 0.97 (d, *J* = 6.6, 3H, CH(C*H*$_3)_2$), - 0.85 (s, 3H, Al-CH_3). ^{13}C{^{1}H}NMR (C_6D_6): δ 189.4($C_{C=N}$), 150.1(C_{Ar}), 148.0(C_{Ar}), 143.1(C_{Ar}), 141.8(C_{Ar}), 141.1(C_{Ar}), 140.0(C_{Ar}), 136.5(C_{Ar}), 132.5(CH_{Ar}), 131.6(CH_{Ar}), 129.3(CH_{Ar}), 129.1(CH_{Ar}), 128.7(CH_{Ar}), 128.3(C_{Ar}), 127.4(CH_{Ar}), 126.4(CH_{Ar}), 125.4(CH_{Ar}), 125.0(CH_{Ar}), 124.6(CH_{Ar}), 60.5(–N–*C*H_2–), 30.8($CH(CH_3)_2$), 29.1($CH(CH_3)_2$), 28.4($CH(CH_3)_2$), 28.1($CH(CH_3)_2$), 27.9($CH(CH_3)_2$), 26.5(–N=C(*C*H_3), 26.4($CH(CH_3)_2$), 26.4($CH(CH_3)_2$), 26.2($CH(CH_3)_2$), 26.0($CH(CH_3)_2$), 25.6($CH(CH_3)_2$), 24.4($CH(CH_3)_2$), 24.0($CH(CH_3)_2$), - 9.87 (AlMe). Anal. Calcd. for $C_{34}H_{46}AlClN_2$: C 74.90; H 8.50; N 5.14. Found: C 74.83; H 8.67 N 5.08.

Synthesis of [1,2-((2,6-^{i}Pr$_2$C$_6$H$_3$N=CH)$_2$-C$_6$H$_4$)AlMeCl]$^+$[AlMe$_x$Cl$_{4-x}$]$^-$ (2)

A flask was charged with γ-diimine (300.0 mg, 0.663 mmol) and $AlMeCl_2$ (1.50 mL, 1.0 M, 1.50 mmol) in toluene (20 mL), following the above procedure, to obtain complex **2** as a yellow solid (733 mg, 70%) ^{1}H NMR (C_6D_6): δ 8.83 (s, 2H, –N=C*H*–), 7.78 (m, 2H, C_6H_4), 7.52 (m, 2H, C_6H_4), 7.10 (m, 2H, C_6H_3), 7.01 (m, 4H, C_6H_3), 3.14 (sept., *J* = 6.3, 2H, C*H*$(CH_3)_2$), 2.77 (sept., *J* = 6.6, 2H, C*H*$(CH_3)_2$), 1.24 (d, *J* = 6.6, 12H, CH(C*H*$_3)_2$), 1.17 (d, *J* = 6.3, 12H, CH(C*H*$_3)_2$), 1.30 (d, *J* = 6.6, 12H, CH(C*H*$_3)_2$), 1.11 (d, *J* = 6.6, 12H, CH(C*H*$_3)_2$), -0.86 (s, 3H, AlMe). ^{13}C{^{1}H}NMR (C_6D_6): δ 182.0($C_{C=N}$), 143.2(C_{Ar}), 142.2(CH_{Ar}), 141.7(C_{Ar}), 141.6(CH_{Ar}),

137.8(C_{Ar}), 131.1(CH_{Ar}), 129.3(CH_{Ar}), 128.7(C_{Ar}), 126.3(CH_{Ar}), 125.6(CH_{Ar}), 30.8 ($CH(CH_3)_2$), 29.8($CH(CH_3)_2$), 29.3($CH(CH_3)_2$), 26.9($CH(CH_3)_2$), 25.5($CH(CH_3)_2$), 23.9($CH(CH_3)_2$), -11.7 (AlMe). Anal. Calcd. for $C_{34}H_{46}Al_2Cl_4N_2$: C 60.18; H 6.83; N 4.13. Found: C 59.83; H 6.65 N 3.99.

Synthesis of $[1,2\text{-}((2,6\text{-}^{i}Pr_2C_6H_3N{=}CH)_2\text{-}C_6H_4)AlCl_2]^{+}[AlCl_4]^{-}$ (3)

A flask was charged with γ-diimine (300.0 mg, 0.663 mmol) and $AlCl_3$ (203.3 mg, 1.525 mmol) in toluene (20 mL), following the above procedure, to obtain complex **3** as a yellow solid (405.4 mg, 85%) ^{1}H NMR (C_6D_6): δ 8.92 (s, 2H, N=C*H*), 7.71 (m, 2H, C_6H_4), 7.47 (m, 2H, C_6H_4), 6.85-7.16 (m, 6H, C_6H_3), 3.00 (sept., *J* = 6.3, 4H, C*H*(CH_3)$_2$), 1.31 (d, *J* = 6.3, 12H, CH(C*H*$_3$)$_2$), 1.29 (d, *J* = 6.3, 12H, CH(C*H*$_3$)$_2$). Anal. Calcd. for $C_{32}H_{40}Al_2Cl_6N_2$: C 53.43; H 5.60; N 3.89. Found: C 53.71; H 5.61 N 3.82.

Synthesis of $[1,2\text{-}((2,6\text{-}^{i}Pr_2C_6H_3N{=}CH)_2\text{-}C_6H_4)AlCl_2]^{+}[Al_2Cl_7]^{-}$ (4)

A flask was charged with γ-diimine (300.0 mg, 0.663 mmol) and $AlCl_3$ (265.2 mg, 1.989 mmol) in toluene (20 mL), following the above procedure, to obtain complex **4** as a yellow solid (480.5 mg, 85%). ^{1}H NMR (C_6D_6): δ 8.59 (s, 2H, N=C*H*), 7.54 (m, 2H, C_6H_4), 7.49 (m, 2H, C_6H_4), 7.20 (dd, *J* = 7.8, 2H, C_6H_3), 7.05 (d, *J* = 7.8, 4H, C_6H_3), 2.88 (sept., *J* = 6.7, 4H, C*H*(CH_3)$_2$), 1.20 (d, *J* = 6.7, 12H, CH(C*H*$_3$)$_2$), 1.13 (d, *J* = 6.7, 12H, CH(C*H*$_3$)$_2$). ^{13}C{^{1}H}NMR (C_6D_6): δ 182.1($C_{C=N}$), 142.6(C_{Ar}), 142.3(CH_{Ar}), 141.3(C_{Ar}), 138.8(CH_{Ar}), 131.8(CH_{Ar}), 128.7(CH_{Ar}), 126.3(C_{Ar}), 30.6 (C*H*(CH_3)$_2$), 26.0(CH(C*H*$_3$)$_2$), 23.6(CH(C*H*$_3$)$_2$).

7.6 X-ray structure determinations

Data were collected at -90 °C on a Nonius Kappa CCD diffractometer, using the COLLECT program.[20] Cell refinement and data reductions used the programs DENZO and SCALEPACK.[21] SIR97[22] was used to solve the structures and SHELXL97[23] was used to refine the structures. ORTEP-3 for Windows[24] was used for molecular graphics and PLATON[25] was used to prepare material for publication. H atoms were placed in calculated positions with U_{iso} constrained to be 1.5 times U_{eq} of the carrier atom for methyl protons and 1.2 times U_{eq} of the carrier atom for all other hydrogen atoms. The structure of complex **1** crystallized as a mixture of two compounds; in addition to the amidoimino ligand one compound has two chlorides while the other contains a methyl group and a chloride atom on the aluminum metal centre. Therefore, at one location there is a chloride atom (Cl2) with 25% site occupancy and a methyl group (C41) with 75% site occupancy.

7.7 Acknowledgments

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7.8 References

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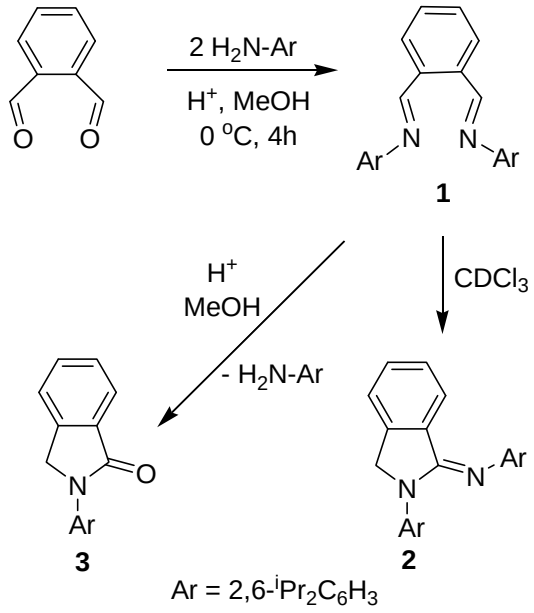
CHAPTER 8

8. Summary, Conclusion and Future Work

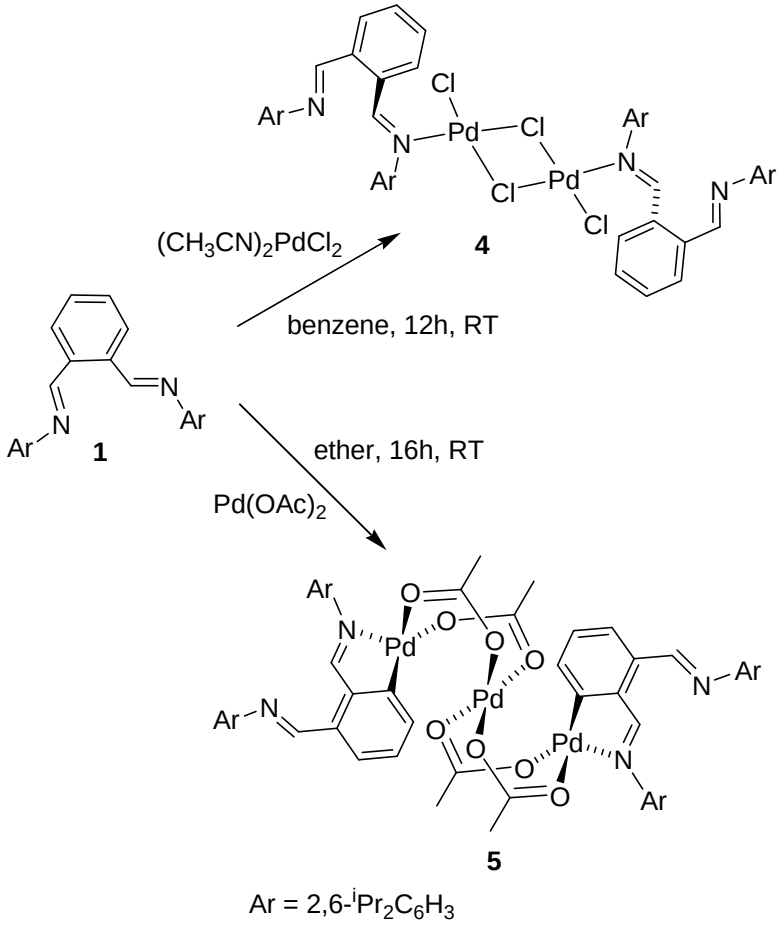
We were initially interested in making a series of γ-diimines analogous to Brookhart's α-diimines, through a condensation reaction of *o*-phthalaldehyde with *di-ortho*-substituted anilines. However, only one γ-diimine ligand, 1,2-(2,6-$^{i}Pr_2C_6H_3N{=}CH)_2$-C_6H_4, (**1**) containing a bulky 2,6-diisopropylaniline was isolated. It was observed that when other anilines with less bulky substituents than 2,6-diisopropylaniline were used, rapid intramolecular cyclization resulted and iminoisoindolines were obtained (Figure 8.1). Interestingly, if **1** is not isolated as a precipitate from the methanolic solution, it further reacts by redissolving back into solution to form the corresponding isoindolinone (**3**), and one equiv of 2,6-diisopropylaniline. Thus, the yield of **1** decreases favoring formation of isoindolinone **3** at longer reaction times. Slow cyclization of γ-diimine **1** to form the corresponding iminoisoindoline **2** in quantitative yield is observed in $CDCl_3$ (Scheme 8.1), which was monitored by ^{1}H NMR spectroscopy (see Chapter 2, Figure 2.5). This result proved that a γ-diimine is an intermediate in the formation of iminoisoindolines from phthaldehyde. γ-Diimine **1** is, however, stable in non-polar organic solvents in the absence of protic acids for prolonged periods. Due to intramolecular cyclization reactions, it is unlikely that γ-diimines will emerge as a new class of ligand comparable to α- and β-diimine analogues. The reactivity of **1** towards group 10 transition metals was investigated. Reaction with $PdCl_2$ did not result in a seven-membered coordination complex, but in non-palladacyclic complex, [(γ-diimine)PdCl(μ-Cl)]$_2$ (**4**). On the other hand, reaction of γ-diimine **1** with $Pd(OAc)_2$ results in C-H activation and formation of an air-stable, five-membered trinuclear palladacyclic species (**5**),

which contains a rare S-shaped $Pd_3(OAc)_4$ core (Scheme 8.2). It is worth noting that in the literature, there are only four reports on structurally characterized compounds with the S-shaped $Pd_3(OAc)_4$ core (see Chapter 2).



Scheme 8.1. Synthesis and intramolecular cyclization of γ-diimine

Complexes **4** and **5** were tested for activity as precatalysts for the Heck and Suzuki coupling reactions. In the Heck coupling reaction of arylbromides and arylchlorides with tert-*n*-butylacrylate, complex **4** gave relatively poor results (TONs of up to 100 and <1, respectively). While in the Suzuki coupling reaction of arylbromides with phenylboronic acid, **4** gave TONs of up to 100. Complex **5** proved to be a more active and stable complex than **4** giving TONs of 10^4 and 86 in the Heck and Suzuki coupling reaction of arylbromides and arylchlorides, respectively.



Scheme 8.2. Formation of γ-diimine-based palladium complexes

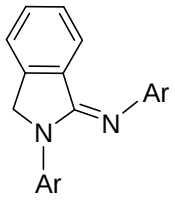


Figure 8.1. General structure of iminoisoindoline ligands

With the above observations in mind, we thought iminoisoindoline ligands could represent a convenient and facile route into the formation of rare imine-based six-membered [CN] palladacycles. We synthesized and characterized a series of air- and moisture-stable iminoisoindoline-based palladacyclic compounds of the general formula, [(R,R'-

iminoisoindoline)Pd{μ-OAc}]$_2$, where R = R' (Figure 8.2, Scheme 8.3). These six-membered palladacyclic complexes were obtained through a simple two-step protocol from commercially available starting materials as analytically pure solids. No palladacycle formation was observed when iminoisoindoline ligand **10**, possessing nitro substituents on the aryl groups of the iminoisoindoline, was reacted with Pd(OAc)$_2$.

The synthesized dinuclear palladacycles **11** and **14** were also found to be active for the Heck and Suzuki C-C coupling reactions. TONs of up to 10^6, 10^5 and 60 were observed for coupling of iodobenzene, *p*-acetylbromobenzene and *p*-chlorobenzaldehyde, respectively in the Heck coupling reaction. In the Suzuki coupling reaction of phenylboronic acid and *p*-acetylchlorobenzene, TONs of up to 100 were recorded.

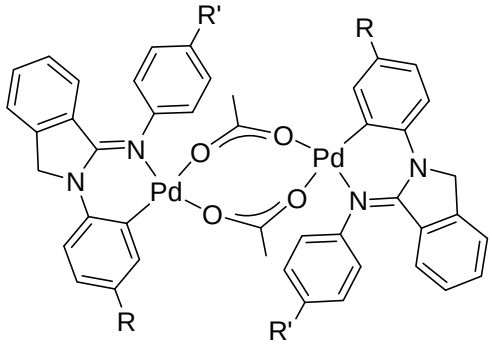
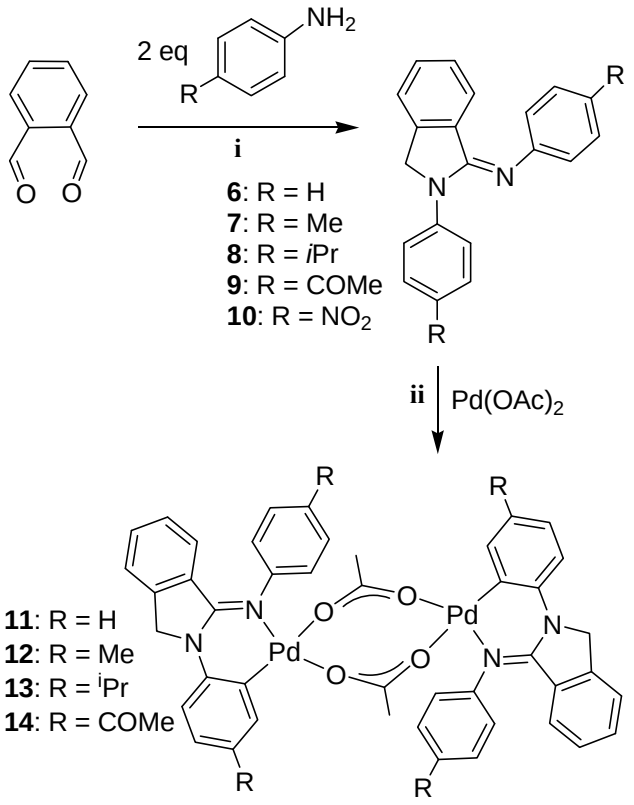


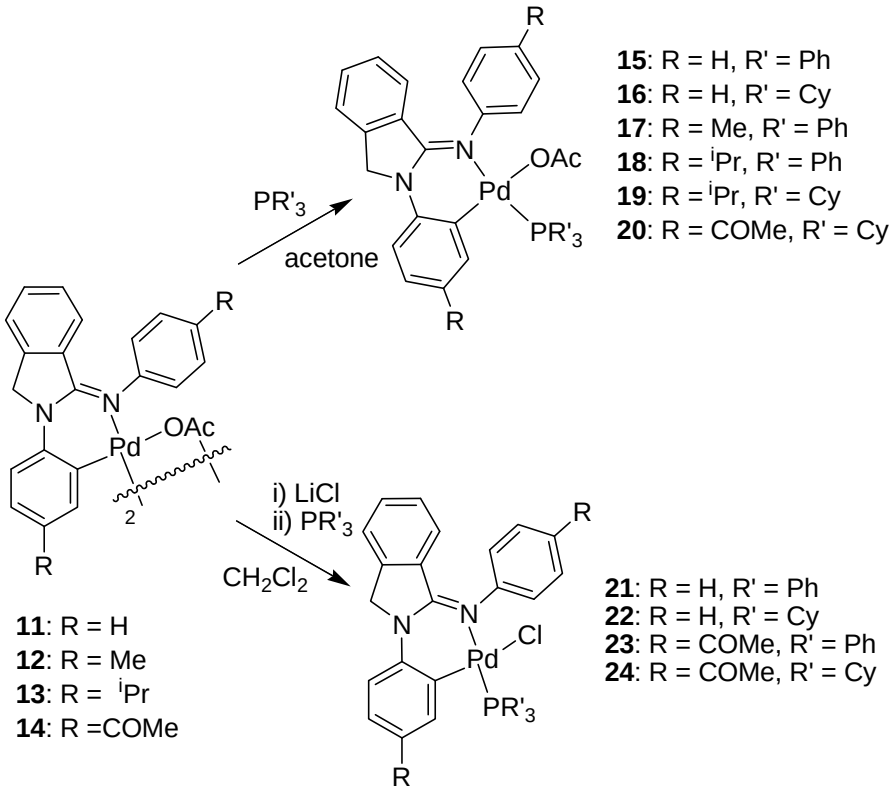
Figure 8.2. Iminoisoindoline-based [CN] palladacycles



Scheme 8.3. Synthesis of dinuclear iminoisoindoline-based [CN] palladacycles

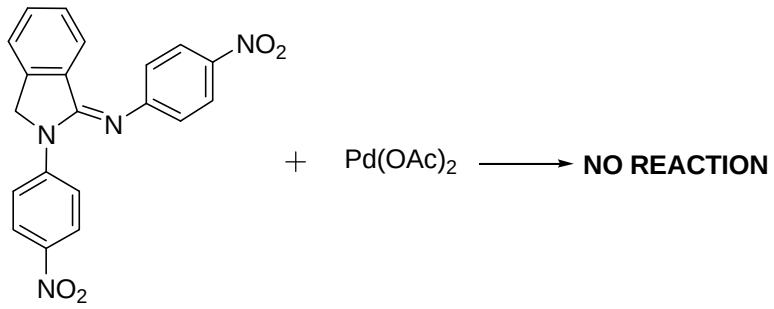
A survey of the literature showed that some mononuclear palladacyclic compounds were more catalytically active in C-C cross coupling reactions than their corresponding dinuclear counterparts. It is for this reason that phosphine-ligated mononuclear palladacycles of the general formula, [Pd(iminoisoindoline)X(PR_3)] (**15-24**), where X = OAc or Cl, and R = Ph or Cy, were prepared (Scheme 8.4). Complexes **15-20**, with acetate terminal ligands, were prepared directly through the reaction of acetate-bridged dinuclear palladacycles (**11-14**) with triphenylphosphine (PPh_3) or tricyclohexylphosphine (PCy_3). Reaction of **11-14** with LiCl followed by PPh_3 or PCy_3 generated complexes **21-24** which have a terminal chloride instead of an acetate ligand. Studies in applications of these mononuclear palladacycles in the C-C coupling reactions are going-on in our

laboratory and their catalytic activities will be compared with those of their dinuclear counterparts.



Scheme 8.4. Synthesis of phosphine-ligated mononuclear [CN] palladacycles

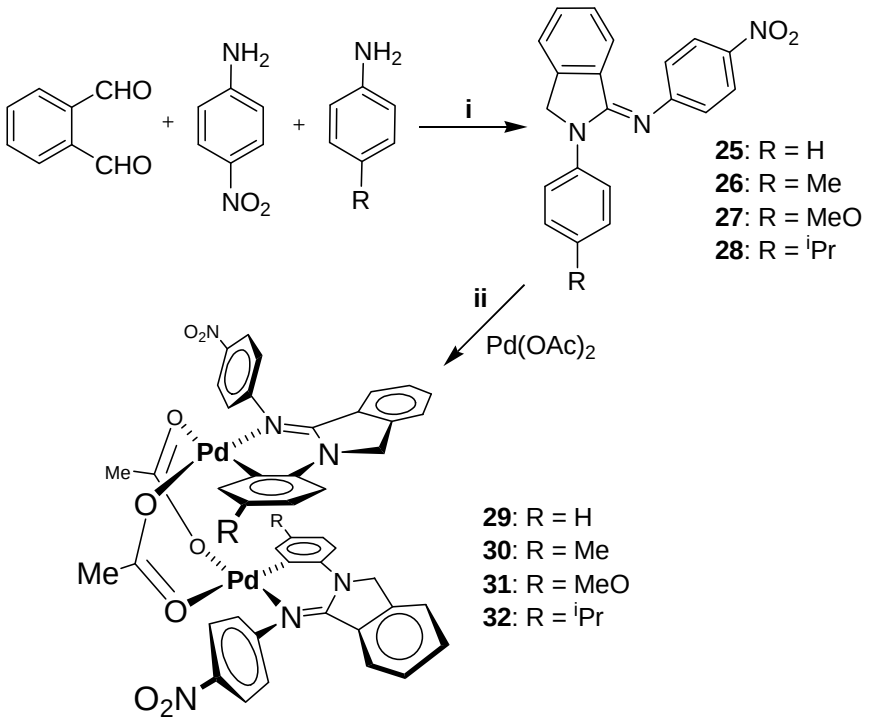
As discussed earlier, reaction of R,R'-diaryliminoisoindoline **10** (R = R' = NO_2) with $Pd(OAc)_2$ did not result in palladacycle formation (Scheme 8.3, Scheme 8.5). This was likely due to the electron withdrawing/deactivating effects of the nitro substituent inhibiting both imine coordination and *ortho*-palladation. Intrigued by this result, we decided to investigate the synthesis of "mixed" Ar,Ar'-diaryliminoisoindoline ligands containing different aryl groups bound to the two nitrogen atoms (R ≠ R', Scheme 8.6) wherein the aryl groups of the mixed diaryliminoisindoline would contain alternatively one nitro group and one neutral or electron donating group in the *para* positions.



10

Scheme 8.5. Attempted synthesis of a palladacycle using ligand **10**

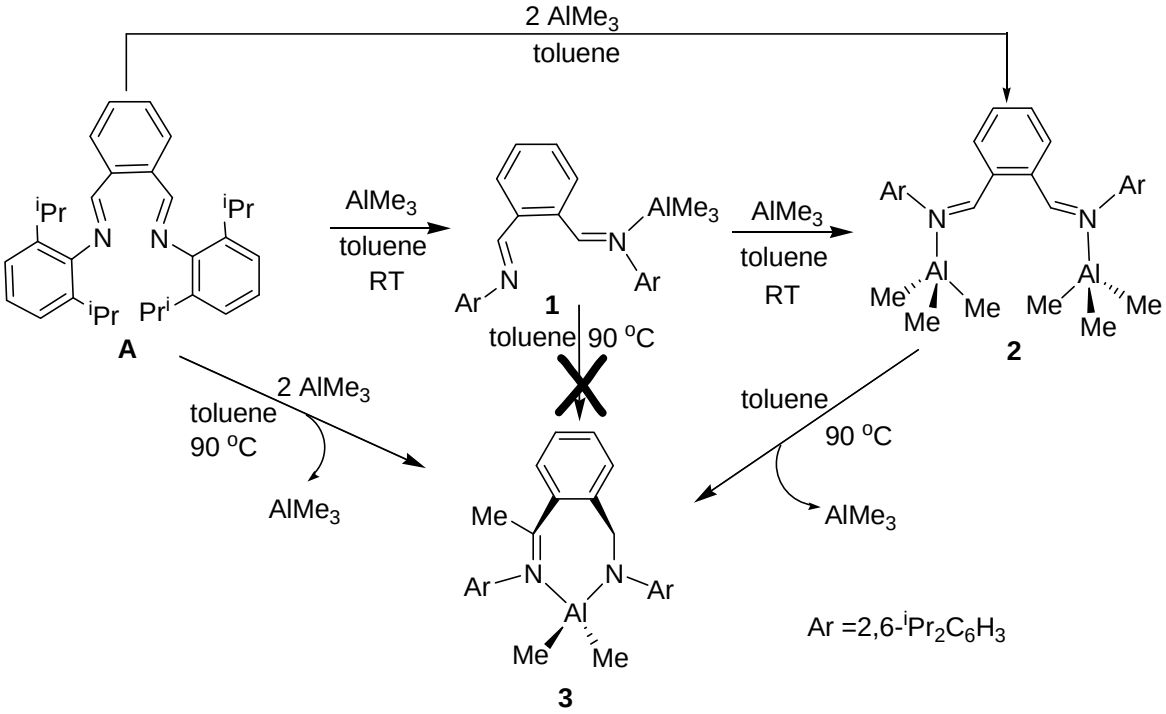
The research question was whether, could "mixed" diaryliminoisoindolines could be synthesized and if so, could palladacycles be synthesized if only one aryl group contained a *para*-nitro functionality? Furthermore, how would this affect C-C coupling activity? Consequently, a one-step, three-component reaction was employed to obtain a series of mixed Ar,Ar'-diaryliminoisoindolines (**25**-**28**). These precipitated out as analytically pure, yellow solids, wherein the more electron withdrawing functionality resides exclusively on the imine nitrogen. Unlike **10**, iminoisoindolines **25**-**28** reacted with $Pd(OAc)_2$ to form corresponding air- and moisture-stable iminoisoindoline-based palladacycles **29**-**32** (Scheme 8.6). All complexes were fully characterized by NMR spectroscopy, mass spectrometry; elemental analysis and molecular structures of some complexes were determined by X-ray crystallographic studies.



Scheme 8.6. Synthesis of palladacycles based on mixed R,R'-diaryliminoisoindoline

Consistent with the overall objective of utilizing γ-diimine ligands to synthesize seven-membered coordination complexes (as discussed in Chapter 2) and also motivated by the work that was conducted by our group and others on the reaction of α-diimines with trimethylaluminum ($AlMe_3$) to obtain (α-amidoimino)$AlMe_2$ complexes (see Chapter 1.8.1), we therefore investigated the factors and reaction conditions by which γ-amidoimino and γ-diimine complexes of alkyl/halide could be synthesized and to explore the reactivity of these complexes in the polymerization of lactones. It was observed that depending on reaction conditions and the type of aluminum reagent employed, diverse aluminum(III) complexes were obtained. Thus, reaction of the γ-diimine with 1 equiv of $AlMe_3$ at ambient temperature gave nonchelating complex **33**, in which $AlMe_3$ is coordinated to one imine nitrogen while the other imine nitrogen remains uncoordinated, as shown in Scheme 8.7. Complex **33** is unchanged even at 90 ºC for 24 h. When

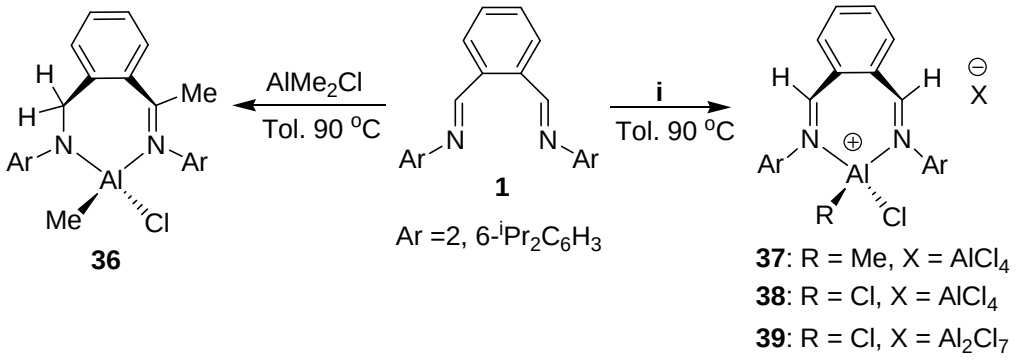
an additional equiv of $AlMe_3$ was added to **33** at ambient temperature, complex **34** was isolated. Complex **34** possesses the γ-diimine ligand which acts as a bidentate, non-chelating ligand bridging the two $AlMe_3$ groups through coordination by the imine moieties. Heating complex **34** to 90 ^oC for 12 h resulted in formation of a neutral seven-membered (γ-amidoimino)$AlMe_2$ complex (**35**). Complex **35** is presumably formed by aluminum coordination, followed by migration of a methyl group to one imine carbon atom, and finally by hydrogen transfer from one imine carbon to the other. Complex **35** was also obtained directly when **1** was reacted with 2 equiv of $AlMe_3$ at 90 ºC for 12 h.



Scheme 8.7. Reaction of a γ-diimine ligand with $AlMe_3$ at different reaction conditions

Reactivity of the γ-Diimine ligand **1** was further investigated with other aluminum species (Me_2AlCl, $MeAlCl_2$, $AlCl_3$) as shown in Scheme 8.8. When the γ-diimine was reacted with 2 equiv of Me_2AlCl in toluene (90 ºC), formation of a neutral seven-membered (γ-

amidoimino)AlMeCl complex (**36**) was observed, likely through the same mechanism as for **35** (Scheme 8.7). On the other hand, reaction of **1** with $MeAlCl_2$ and $AlCl_3$ form cationic aluminum complexes (**37**, **38** and **39**), with different counter ions depending on the aluminum species and stoichiometry employed. Cationic aluminum complex, $[(\gamma\text{-Diimine})AlMeCl]^+$ **(37)** with a tetrachloroaluminate, $[AlCl_4]^-$ counter ion was obtained from the reaction of 2 equiv of $MeAlCl_2$ with **1** at 90 ºC for 12 h. In the same manner, reaction of **1** with 2 or 3 equiv of $AlCl_3$ results in $[(\gamma\text{-diimine})AlCl_2]^+$ complex possessing tetrachloroaluminate, $[AlCl_4]^-$ (**38**) and heptachlorodialuminate, $[Al_2Cl_7]^-$ (**39**) as counter ions, respectively. The second equivalent of $AlMe_xCl_{3-x}$ (x = 0, 1) is required in order to abstract a chloride, thereby generating a more Lewis acidic aluminum centre that forces the diimine ligand to coordinate in a chelating fashion. This is the first time we have observed the γ-diimine ligand coordinating in a chelating neutral manner.



Scheme 8.8. Synthesis of neutral (γ-amidoimino)Al(Me)Cl and cationic $[(\gamma\text{-diimine})AlRCl]^+$ complexes i: 2 equiv $MeAlCl_2$ (37), 2 equiv $AlCl_3$ (38), 3 equiv $AlCl_3$ (39), in toluene at 90 ºC

Molecular structures of all aluminum complexes were determined by X-ray crystallography and in addition, other techniques such as ^1H NMR, ^{13}C NMR and elemental analysis were employed to fully characterize these complexes.

Catalytic studies of C-C coupling reactions, which are aimed at comparing activities of dinuclear palladacycles (**11-14** and **29-32**) with that of mononuclear phosphine-ligated palladacycles (**16-24**) are future research areas. In addition, the exploration into the use of neutral (γ-amidoimino)$AlMe_2$ **35-36** and cationic γ-diimine aluminum complexes **37-39** in the ring-opening polymerization of lactones/lactides is being investigated in our laboratory.